

Endurance exercise and atrial fibrillation

Atrial fibrillation among Norwegian veteran endurance athletes
and the association between endurance exercise and
risk of atrial fibrillation

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CONTENTS

Acknowledgements.....	6
Funding.....	8
Abbreviations.....	9
List of papers.....	10
Summary.....	11
Norsk sammendrag.....	13
 1. Introduction.....	 15
1.1 Physical activity and endurance exercise.....	15
1.1.1 Definitions.....	15
1.1.2 Physical activity, endurance exercise and health outcomes.....	15
1.1.3 Adverse effects of endurance exercise and sport practice.....	16
1.2 Atrial fibrillation.....	17
1.2.1 Definition, classification and natural course.....	17
1.2.2 Epidemiology.....	17
1.2.3 Symptoms.....	19
1.2.4 Consequences.....	19
1.2.5 Etiology and risk factors.....	19
1.2.6 Atrial flutter.....	21
1.3 Endurance exercise, sport practice and risk of atrial fibrillation.....	21
1.3.1 Previous studies of Norwegian cross-country skiers.....	21
1.3.2 Previous studies of atrial fibrillation in athletes.....	21
1.3.3 Previous studies of the association between endurance exercise and the risk of atrial fibrillation.....	21
1.3.4 Meta-analysis and reviews.....	24
1.3.5 Summary of previous studies.....	24
 2 Aims of this thesis.....	 25
 3 Materials.....	 26
3.1 The Birkebeiner cross-country ski race.....	26
3.2 The Birkebeiner Ageing Study.....	26
3.2.1 The Birkebeiner Ageing Study.....	26
3.2.2 The Tromsø Study.....	27

3.3 The Birkebeiner Atrial Fibrillation Study.....	27
3.3.1 The cohort of veteran cross-country skiers.....	28
3.3.2 The Oslo Health Study.....	28
4 Methods.....	30
4.1 Assessment of the main outcome atrial fibrillation.....	30
4.1.1 Self-reported atrial fibrillation.....	30
4.1.2 Atrial fibrillation confirmed by ECG.....	30
4.2 Assessment of other outcomes.....	31
4.2.1 Leisure-time physical activity and endurance exercise.....	31
4.2.2 Symptoms, drug use and subjective health.....	31
4.3 Assessment of the main exposure endurance exercise.....	32
4.4 Covariates.....	32
4.5 Statistical analyses.....	33
4.6 Ethical considerations.....	34
5 Results.....	35
5.1 Paper I: Endurance sport practice as a risk factor for atrial fibrillation.....	35
5.2 Paper II: Prolonged endurance exercise is associated with a graded increased risk of atrial arrhythmias in men.....	36
5.3 Paper III: Prolonged endurance exercise might be associated with atrial fibrillation in women.....	37
5.4 Paper IV: The majority of veteran athletes still engage in regular physical activity and exercise after the onset of atrial fibrillation.....	37
6 Discussion.....	38
6.1 Methodological considerations.....	38
6.1.1 Study design.....	38
6.1.2 Atrial fibrillation measurements.....	39
6.1.3 Measurements of other endpoints.....	41

6.1.4	Measurement of endurance exercise.....	42
6.1.5	Measurements of co-morbid conditions and confounding.....	42
6.2	Discussion of the main results.....	42
6.2.1	Endurance sport practice as a risk factor for atrial fibrillation.....	42
6.2.2	Prolonged endurance exercise and risk of atrial fibrillation.....	43
6.2.3	Prolonged endurance exercise and risk of atrial fibrillation in women.....	44
6.2.4	Characteristics of atrial fibrillation in veteran athletes.....	45
6.2.5	Physical activity and endurance exercise in veteran athletes with atrial fibrillation.....	46
6.2.6	General discussion.....	46
7	Conclusions.....	50
8	Consequences of this thesis and suggestions for future research.....	51
8.1	Consequences of this thesis.....	51
8.2	Suggestions for future research.....	51
9	References.....	53
10	Papers.....	64
11	Appendix: Questionnaires	

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ABBREVIATIONS

AF = Atrial fibrillation

AFL = Atrial flutter

BMI = Body Mass Index

aOR = Adjusted odds ratio

aRD = Adjusted risk difference

CHD = Coronary heart disease

CI = 95% confidence interval

ECG = Electrocardiogram

HR = Hazard ratio

Kcal = Kilocalories

NYHA = New York Heart Association

OAC = Oral anticoagulant

OR = Odds ratio

PA = Physical activity

PPV = Positive predictive value

RD = Risk difference

RR = Relative risk

SCD = Sudden cardiac death

LIST OF PAPERS

- I. **Increased risk of atrial fibrillation among elderly Norwegian men with a history of long-term endurance sport practice**
Myrstad M, Løchen ML, Graff-Iversen S, Gulsvik AK, Thelle DS, Stigum H, Ranhoff AH.
Scand J Med Sci Sports. 2014; 24, e238-e244.
doi: 10.1111/sms.12150. Epub 2013 21 Nov.
- II. **Effect of years of endurance exercise on risk of atrial fibrillation and atrial flutter**
Myrstad M, Nystad W, Graff-Iversen S, Thelle DS, Stigum H, Aarønæs M, Ranhoff AH.
Am J Cardiol. 2014;114:1229-33.
doi: 10.1016/j.amjcard.2014.07.047. Epub 2014 Jul 30.
- III. **Letter to the editor: Does endurance exercise cause atrial fibrillation in women?**
Myrstad M, Aarønæs M, Graff-Iversen S, Nystad W, Ranhoff AH.
Int J Cardiol. 2015;184:431-432.
doi:10.1016/j.ijcard.2015.03.018. Epub 2015 Mar 3.
- IV. **Physical activity, symptoms, medication and subjective health among veteran endurance athletes with atrial fibrillation**
Myrstad M, Aarønæs M, Graff-Iversen S, Ariansen I, Nystad W, Ranhoff AH.
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SUMMARY

Background

Atrial fibrillation (AF) is the most common clinically relevant cardiac arrhythmia. AF is associated with reduced functional capacity and other symptoms, drug use, poor subjective health, increased risk of ischemic stroke and increased mortality.

Physical activity (PA) reduces the risk of cardiovascular diseases and has multiple beneficial health effects, but male endurance athletes seem to have an increased risk of AF. Few studies, however, have investigated the association between prolonged endurance exercise and the risk of AF, and this association has not been studied in women previously. The number of individuals aged >40 years that engage in endurance sports events is increasing, but few studies have investigated the association between endurance sport practice and risk of AF in veteran athletes. Furthermore, AF and its consequences have been just sporadically described in veteran athletes previously.

The main aims of this thesis were 1) to investigate endurance sport practice as a risk factor for AF in veteran athletes (paper I), 2) to investigate the association between prolonged regular endurance exercise and risk of AF in men (paper II), 3) to investigate the association between prolonged regular endurance exercise and risk of AF in women (paper III), and 4) to characterize AF and investigate PA, endurance exercise, symptoms, drug use and subjective health in veteran athletes with AF (paper IV).

Methods

Paper I is based on the Birkebeiner Ageing Study. In this cross-sectional study, 509 out of 607 invited men (84%) aged ≥ 65 years who took part in the 54-kilometer Birkebeiner cross-country ski race in 2009 or 2010 participated. These veteran athletes were compared to 1768 out of 2757 invited men aged ≥ 65 years (68%) participating in a population-based health study. The main outcome AF was self-reported by questionnaires. The main exposure was endurance sport practice, defined as participating in the Birkebeiner race. We calculated adjusted risk differences (aRDs) for AF with 95% confidence intervals (CIs) using a linear regression model.

In the papers II and III, we investigated the association between prolonged regular endurance exercise and the risk of AF in men and women, respectively. These papers are based on a second study, the Birkebeiner Atrial Fibrillation Study. The study population of this retrospective cohort study comprised two distinct cohorts: 1) Veteran athletes aged ≥ 53 years who had participated in the Birkebeiner race in 1999, and 2) participants in the same group in a population-based health study. In total, 5390 out of 7500 invited men and women (72%) took part in the Birkebeiner Atrial Fibrillation Study. In the study of men (paper II), the main outcome was AF and atrial flutter (AFL) confirmed by electrocardiograms (ECGs) in a review of medical records. Due to the low number of confirmed AF cases among female participants, self-reported AF was the main outcome in the analysis of women (paper III). The main exposure, years of regular endurance exercise was self-reported by questionnaires. Regular endurance exercise was defined as exercise for at least 30 minutes ≥ 3 times per week with the purpose of

increasing physical endurance capacity. Adjusted odds ratios (aORs) for AF with CIs were calculated using weighted logistic regression models.

Also paper IV is based on the Birkebeiner Atrial Fibrillation Study. In this study, we characterized AF in detail among 140 veteran skiers and 118 individuals from the general population with confirmed AF. Furthermore, we investigated engagement in PA and endurance exercise after the onset of AF, palpitations, functional capacity, drug-use and subjective health in veteran athletes with AF and in the general AF population.

Results

The prevalence of self-reported AF in the Birkebeiner Ageing Study was 13.2% in the veteran athletes and 11.6% in the men from the general population. After multivariable adjustment for age, height, body mass index (BMI), coronary heart disease (CHD), hypertension, diabetes mellitus, smoking, alcohol consumption, leisure-time PA during the past year and education, endurance sport practice was associated with an added risk of AF of 6 percent points (pp) (aRD 6.0 (CI 0.8-11.1)), corresponding to an aOR of 1.90 (CI 1.14-3.18).

In the Birkebeiner Atrial Fibrillation Study, the prevalence of self-reported AF was 12.5% among the male veteran athletes. After multivariable adjustment for age, height, concomitant heart disease, hypertension, diabetes mellitus and cohort affiliation, years of regular endurance exercise was associated with a gradually increased risk of both AF and AFL. Per 10 years of exercise, the aOR was 1.16 (CI 1.06-1.29) for AF and 1.42 (CI 1.20-1.69) for AFL. In stratified analyses, the associations were significant both in the veteran athletes and in the men from the general population. Men who had exercised regularly for ≥ 40 years had an aOR for AF of 1.94 (CI 1.19-3.14) compared to men who had never exercised regularly.

The prevalence of self-reported AF among female veteran skiers was 8%. After multivariable adjustment for age, BMI, concomitant heart disease, hypertension, diabetes mellitus and cohort affiliation, women who had exercised regularly for ≥ 40 years had an increased risk of AF of borderline significance (aOR 2.18 (CI 0.94-5.06)) compared to women who had never exercised regularly.

Among veteran athletes with AF, 52% had paroxysmal, 23% had persistent and 24% had permanent AF. AF was associated with poor subjective health, but 89% of the veteran athletes were physically active and 64% engaged in regular endurance exercise after the onset of AF. While 59% had experienced palpitations during the past year, 32% reported reduced functional capacity. Two out of three with AF and an estimated CHA₂DS₂-VASC score ≥ 2 used oral anticoagulants (OACs).

Conclusions

In conclusion, 1) endurance sport practice seemed to be a risk factor for AF in men aged ≥ 65 years, 2) years of regular endurance exercise was associated with a gradually increased risk of both AF and AFL in men, 3) our study indicated that prolonged endurance exercise might be associated with AF also in women, and 4) AF was associated with poor subjective health, but the vast majority of veteran athletes engaged in regular PA and endurance exercise also after the onset of AF.

NORSK SAMMENDRAG

Innledning

Atrieflimmer (AF) er den vanligste hjerterytmeforstyrrelsen som har klinisk betydning. AF er forbundet med redusert fysisk yteevne og andre symptomer, medisinbruk, dårlig selvpoplevd helse, økt risiko for hjerneslag og økt dødelighet.

Fysisk aktivitet (FA) reduserer risikoen for hjerte- og karsykdom og er forbundet med en rekke gunstige helseeffekter, men mannlige idrettsutøvere i utholdenhetsidretter ser ut til å ha en økt risiko for AF. Få studier har undersøkt sammenhengen mellom langvarig utholdenhets trening og risiko for AF og tidligere studier har ikke funnet noen sammenheng mellom deltakelse i utholdenhetsidrett og risiko for AF blant kvinner. Stadig flere personer >40 år deltar i Birkebeinerrennet, maratonløp og lignende arrangementer, men FA og trening, symptomer, medisinbruk og selvpoplevd helse blant eldre birkebeinere med AF har ikke blitt kartlagt tidligere.

Hensikten med studiene i denne avhandlingen var 1) å undersøke deltakelse i utholdenhetskonkurranser som risikofaktor for AF blant eldre birkebeinere (artikkel I), 2) å undersøke sammenhengen mellom langvarig regelmessig utholdenhets trening og risiko for AF blant menn (artikkel II), 3) å undersøke sammenhengen mellom langvarig regelmessig utholdenhets trening og risiko for AF blant kvinner (artikkel III), og 4) å beskrive AF og undersøke deltakelse i FA og utholdenhets trening, symptomer, medisinbruk og selvpoplevd helse blant eldre birkebeinere (personer ≥ 53 år som tidligere hadde deltatt i Birkebeinerrennet (artikkel IV).

Metoder

Artikkel 1 er basert på Birkebeiner Aldringsstudien. Total 509 av 607 inviterte menn (84%) ≥ 65 år som var med i Birkebeinerrennet i 2009 eller 2010, deltok i denne tverrsnittstudien. Birkebeinerne ble sammenlignet med 1768 av 2757 inviterte menn ≥ 65 år (68%) som hadde deltatt i en helseundersøkelsen i Tromsø (Tromsøundersøkelsen). Studiens endepunkt var selv-rapportert AF og eksponeringen var deltakelse i Birkebeinerrennet. Justerte risikodifferanser (aRDs) med 95% konfidensintervaller (KIs) ble beregnet med en lineær regresjonsmodell.

I artikkel II undersøkte vi sammenhengen mellom langvarig regelmessig utholdenhets trening og risiko for AF blant menn, og i artikkel III ble den samme sammenhengen undersøkt blant kvinner. Begge artiklene er basert på Birkebeiner Atrieflimmer Studien. Studiepopulasjonen i denne retrospektive kohortstudien er sammensatt av to uavhengige kohorter: 1) Menn og kvinner ≥ 53 år som deltok i Birkebeinerrennet i 1999, og 2) deltakere i en helseundersøkelse i Oslo (Osloundersøkelsen). Til sammen 5390 av de 7500 inviterte (72%) fra de to kohortene deltok i Birkebeiner Atrieflimmer Studien. AF og atrieflutter (AFL) bekreftet med elektrokardiogram under en gjennomgang av sykehusjournaler var hovedendepunktene i artikkel II. Fordi antallet kvinner med tilgjengelig journal var lavt, ble selv-rapportert AF valgt som endepunkt i studien av kvinner (artikkel III). Eksponeringen var selv-rapportert antall år med regelmessig utholdenhets trening. Regelmessig utholdenhets trening ble definert som utholdenhets trening av minst 30 minutters

varighet minst tre ganger i uken med mål om å forbedre utholdenhet. Justerte odds ratioer (aORs) med KIs ble beregnet med vektet logistisk regresjon.

Også artikkel IV er basert på Birkebeiner Atrieflimmer Studien. I denne artikkelen beskrev vi AF blant 140 birkebeinere og 118 personer fra den generelle befolkningen (Oslo-undersøkelsen) med bekreftet AF. Vi undersøkte også deltakelse i PA og utholdenhetstrening blant personer med AF, samt symptomer som hjertebank og redusert fysisk yteevne, medisinbruk og selvopplevd helse.

Resultater

Forekomsten av AF i Birkebeiner Aldringsstudien var 13.2% blant birkebeinerne og 11.6% i utvalget fra Tromsø-undersøkelsen. Etter justering for alder, kroppshøyde, kroppsmasseindeks (KMI), koronar hjertesykdom, høyt blodtrykk, diabetes mellitus, røyking, alkoholvaner, FA siste år og utdanningsnivå, var deltakelse i Birkebeinerrennet forbundet med et tillegg i risiko for AF på 6 prosentpoeng (pp) (aRD 6.0 (KI 0.8-11.1)). Dette tilsvarer en aOR på 1.90 (KI 1.14-3.18).

I Birkebeiner Atrieflimmer Studien var forekomsten av selv-rapportert AF blant de mannlige birkebeinerne 12.5%. Etter justering for alder, kroppshøyde, annen hjertesykdom, høyt blodtrykk, diabetes mellitus og kohort, var antall år med regelmessig utholdenhetstrening forbundet med en gradert økt risiko for både AF og AFL. Per tiår med trening var aOR 1.16 (KI 1.06-1.29) for AF og 1.42 (KI 1.20-1.69) for AFL. I stratifiserte analyser var sammenhengen signifikant både blant birkebeinerne og i utvalget fra Oslo-undersøkelsen. Menn som hadde trent regelmessig i ≥ 40 år hadde en aOR for AF på 1.94 (KI 1.19-3.14) sammenlignet med menn som aldri hadde trent regelmessig.

Forekomsten av selv-rapportert AF blant de kvinnelige birkebeinerne var 8%. Etter justering for alder, KMI, annen hjertesykdom, høyt blodtrykk, diabetes mellitus og kohort, hadde kvinner som hadde trent regelmessig i ≥ 40 år en grensesignifikant forhøyet risiko for AF (aOR 2.18 (KI 0.94-5.06)) sammenlignet med kvinner som aldri hadde trent regelmessig.

Blant birkebeinerne med AF hadde 52% paroksysmal AF (anfall som går over av seg selv), 23% hadde persistent AF (anfall som går over etter behandling) og 24% permanent AF. AF var forbundet med dårlig selvopplevd helse, men 89% av birkebeinerne var fysisk aktive og 64% drev fortsatt med regelmessig utholdenhetstrening etter at de hadde fått AF. Mens 59% rapporterte å ha hatt hjertebank siste år, hadde 32% opplevd redusert fysisk yteevne. To av tre med AF og en estimert CHA₂DS₂-VASc ≥ 2 brukte orale antikoagulantia.

Konklusjoner

1) Deltakelse i Birkebeinerrennet så ut til å være en risikofaktor for AF blant menn ≥ 65 år, 2) antall år med regelmessig utholdenhetstrening var assosiert med en gradert økt risiko for både AF og AFL hos menn, 3) vår studie indikerte at langvarig utholdenhetstrening kan være forbundet med en økt risiko for AF også blant kvinner, og 4) AF var forbundet med dårlig selvopplevd helse, men majoriteten av birkebeinerne var regelmessig fysisk aktive og deltok i utholdenhetstrening også etter at de hadde fått AF.

1 INTRODUCTION

1.1 Physical activity and endurance exercise

1.1.1 Definitions

In terms of health-related research *PA* is defined as any bodily movement produced by skeletal muscles that results in energy expenditure [1]. The energy expenditure varies continuously from low to high and the lowest energy expenditure is seen during sedentary activities that involve sitting [2]. In research, PA is often categorized into occupational or leisure-time PA. Leisure-time PA covers households tasks like for example gardening, and recreational activities like cycling, walking and even regular exercise, and has traditionally been divided into 4 subcategories: Sedentary, light, moderate and high PA [3].

While PA covers bodily movement at any level, *exercise* is defined as planned, structured and repetitive bodily movement with the purpose to improve or maintain physical fitness [1]. The goal of *endurance exercise* is the improvement of physical capacity by increasing the maximum oxygen consumption. Endurance sports like cross-country skiing are characterized by a high dynamic component, defined in terms of a high achieved percent of maximal oxygen consumption and a high cardiac output during activity [4]. In this thesis, *regular endurance exercise* is defined as exercise for ≥ 30 minutes at least three times per week with the purpose of increasing physical endurance capacity. *Prolonged endurance exercise* is used to describe such exercise that has been continued for many years.

Over the last decades, there has been an increased participation in endurance sports events like marathons, triathlons and long-distance cross-country ski races [5, 6]. In this thesis the term *endurance sport practice* is used to describe participation in such endurance sports events.

There term *athlete* is widely used, but there is a lack of a clear-cut and uniform definition in previous studies [7]. *Former* or *veteran athletes* have previously been used to describe former top-level athletes aged 46-72 years [8, 9]. In this thesis we use the term *veteran athletes* to describe individuals who have participated in a long-distance cross-country ski race when aged ≥ 40 years.

1.1.2 Physical activity, endurance exercise and health outcomes

Already more than 2,000 years ago Hippocrates stated that “...the sick will of course profit to a great extent from gymnastics with regard to the restoration of their health, and the healthy will profit with regard to its maintenance, and those who exercise will profit with regard to the maintenance of their well-being and a lot more” [10].

After the second world war, Jeremy N. Morris and his colleagues were the first to investigate the association between physical inactivity and risk of cardiovascular disease and death with modern epidemiological methods [11]. In a study conducted among >31 000 male employees of the London Transport Executive, Morris *et al*, demonstrated

that the inactive drivers of the London buses had about the double age-adjusted rate of the conductors who ran up and down the stairs of the buses to sell tickets, of both fatal and non-fatal CHD. Since, knowledge regarding associations between PA and various health outcomes has been added and today PA and exercise are recognized as cornerstones of the primary prevention of many diseases and conditions. Reduced mortality is the best documented among the many beneficial health effects of PA [12-17], but also a reduced risk of cardiovascular diseases by regular PA is well established [18-24]. Furthermore, PA reduces the risk of stroke and cardiovascular risk factors like hypertension, diabetes mellitus and obesity [25-33], and a reduced risk of cancer by PA has been demonstrated [34-38].

Because the prevalence of risk factors increases with increasing age, the potential benefits of PA and exercise might be highest in the oldest age groups. In a recent Norwegian study, the relative importance of PA as health promoting factor increased with increasing age, when compared to other cardiovascular risk factors [39]. Improved cognitive functions and reduced risk of dementia, reduced risk of depression, increased muscle strength and volume, improved mobility, increased bone density, and reduced risk of falls and fractures are among other benefits of PA observed in studies of old individuals [40, 41].

Finally, although rest was recommended for patients with established CHD for decades, exercise is today the most important component of cardiac rehabilitation and secondary prevention of many diseases [42, 43].

It seems to be an inverse dose-response relationship between PA and health outcomes: Increased levels of PA are associated with lower mortality and morbidity [44]. The largest improvement might be achieved by moving from inactive to active, while less benefit could be expected by increasing the activity level from moderate to high [45, 46]. However, also endurance exercise is associated with reduced mortality [47-50]. In a recently published study among >44,000 men in the United States, increasing amounts of high PA remained inversely associated with the risk of cardiovascular and other diseases, even among the men in the highest categories of exercise [51]. Also elite athletes have lower mortality rates than the general population [52]. On the other hand, in a cohort study of Dutch male non-elite participants in a long-distance speed skating event, the mortality was lower among those who participated in the recreational tour compared to those who competed in the race [50]. Recently, a Danish study suggested a U-shaped association between dose of jogging and mortality [53]. Thus, the optimal dose of exercise in terms of health promotion is controversial, and there is a need for studies that include individuals exposed to various levels of exercise [46, 54].

1.1.3 Adverse effects of endurance exercise and sport practice

In general, exercise has few harmful side-effects. Some activities like alpine skiing, bike cycling, boxing and other contact sports are related to an increased risk of traumatic injuries, and running frequently cause musculoskeletal overuse-injuries [55]. But most sports injuries are minor and have relatively little impact on the general health condition. It is well known that endurance sport practice might induce life-threatening ventricular arrhythmias and cause sudden cardiac death (SCD). In most cases of SCD in athletes, however, there is an underlying cardiovascular abnormality [56-58]. The incidence of SCD in athletes might be expected to increase, as the number of older and

less fit individuals that engage in endurance sport events is increasing [5, 6, 59]. In a Swedish study, cross-country skiers participating in the 90-kilometer Vasaloppet had an increased risk of acute mortality during the race, but the authors of the paper concluded that this risk was by far outweighed by the long-term protective effects on mortality of PA and exercise [49].

1.2 Atrial fibrillation

1.2.1 Definition, classification natural course

AF was first described in humans by Einthoven in 1906 [60]. AF is the most common sustained cardiac arrhythmia and characterized by absolutely irregular RR intervals in the ECG. The precise underlying mechanisms are still under debate [61], but the arrhythmia is mainly initiated by triggers located in the pulmonary veins and maintained due to micro-circuits of electrical waves, usually referred to as micro-re-entries or rotors [62]. AF is usually classified into three or five subtypes. In clinical practice in Norway three subtypes are commonly used:

- 1) Paroxysmal - self-terminating AF, usually within 48 hours.
- 2) Persistent - AF episodes that last longer than seven days or require termination by cardioversion with drugs or by direct current cardioversion.
- 3) Permanent – AF that is present permanently.

In addition, the 2012 focused update of the European Society of Cardiology (ESC) guidelines recommend to use two other subtypes [63]:

- 4) First-time diagnosed AF, and
- 5) Long-lasting persistent AF that has lasted for more than one year.

The natural course of the arrhythmia is a progression from short and rare episodes to longer lasting and more frequent attacks. AF paroxysms vary over time and between individuals, both in terms of frequency, duration and symptoms. Only 2-3% of all AF patients remain with paroxysmal AF over time [64], and AF typically develops into a more permanent arrhythmia with increasing age. Thus, the proportions of the AF subtypes vary dependent on the studied population. In a prevalence study among 75-years old Norwegians, 11% of the individuals with AF had first-time diagnosed AF, 36% had paroxysmal, 1% had persistent and 52% had permanent AF [65].

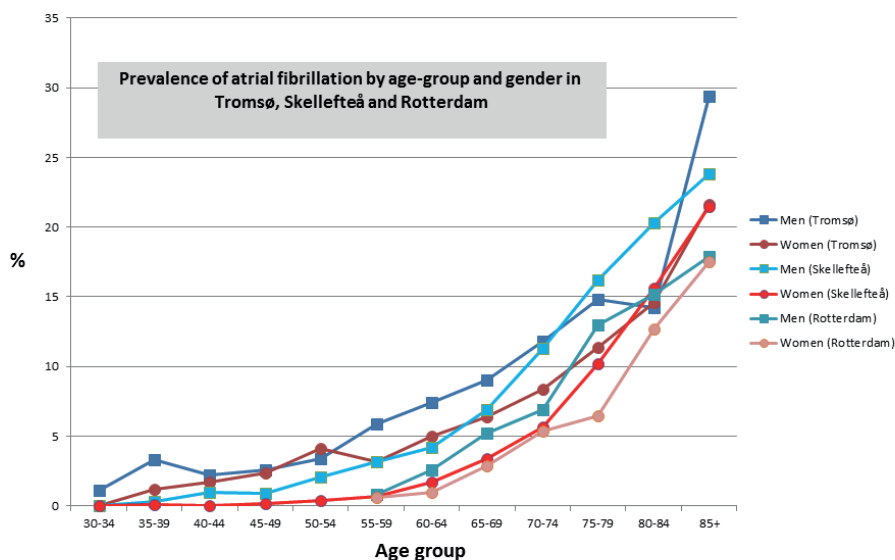
1.2.2 Epidemiology

The overall prevalence of AF in the general western population is 1-2 %, but the prevalence increases with increasing age [66]. The prevalence is less than 0.5% before the age of 50 years, but increases steeply from the age of around 65 to around 10% in individuals aged 75 years, and more than 15% in those aged over 80 years [67, 68]. Figure 1 shows the prevalence of AF by age group in men and women in three population-based studies conducted in Tromsø, Skellefteå (Northern Sweden) and Rotterdam. The prevalence was highest in the Tromsø study, where AF was self-reported (unpublished data from the Tromsø Study). Similar to CHD [69], AF seems to occur 5-10

years later in women than in men. The prevalence was higher in the Swedish study from 2010 compared to the Rotterdam study conducted around 20 years earlier. Due to increased survival after acute coronary syndrome, increased prevalence of risk factors for AF like obesity and diabetes and the ageing population, the prevalence of AF might be increasing over time, with estimates indicating a doubled prevalence within the next 50 years [66, 70].

There are no complete AF prevalence data available for the Norwegian population. Tveit, *et al*, found a prevalence of 10% in a population of 75-years old Norwegians , 6% in women and 15% in men [65]. In 2011, Tveit estimated that 73,500 Norwegians had AF and that the prevalence is likely to be doubled until 2040 [71].

Figure 1. Prevalence of atrial fibrillation by age group and gender in Tromsø (2007-08) (unpublished data from the Tromsø study), Skellefteå (Northern Sweden) (2010) and Rotterdam (1990-93), modified [67, 68].



1.2.3 Symptoms

The most commonly reported symptom among AF patients is palpitations [72]. In this thesis *palpitations* are defined as sudden changes in the heart rate or heart rhythm that are perceived by the patient. Other commonly reported symptoms are dyspnea, chest pain, dizziness, fatigue, anxiety, exercise intolerance and reduced functional capacity [72]. In this thesis *reduced functional capacity* is defined as limitations in physical functions due to symptoms like dyspnea, chest pain or fatigue related to the heart disease, as measured by the New York Heart Association (NYHA) classification. Furthermore, AF is related to poor subjective health and drug use [73, 74]. In previous studies, patients with paroxysmal AF were more likely to be symptomatic than patients with permanent AF [74]. Symptoms in AF patients might be caused by the arrhythmia itself or by concomitant conditions. As heart failure, CHD, heart valve diseases and other co-morbidities are common in AF patients, the causes of symptoms are probably multifactorial in many individuals [72]. The symptom burden is therefore likely to vary dependent on the studied population.

1.2.4 Consequences

AF is associated with increased risk of all-cause mortality, stroke and heart failure [75]. In the Framingham Study, AF was associated with an aOR of death of 1.5 (CI 1.2 – 1.8) [76], and among Swedish AF patients, the standardized mortality ratio was 1.6 (CI 1.4 – 1.8) compared to the general population [77]. In this study, the increased mortality appeared to be related to concomitant cardiovascular risk factors, but in another Swedish study, AF was found to be an independent risk factor for mortality, even after adjustment for co-morbidity [78]. In another study, the relative risk (RR) for death in individuals with AF was higher in women than in men (RR 2.2 versus 1.5) [75].

In a population of >186,000 AF patients with a mean age of 79.5 years and a high prevalence of co-morbid conditions, death was the most frequent major outcome within the first five years after the diagnosis of AF [79]. The cumulative incidence of death was 19.5% after 1 year and 48.8% after 5 years. After 5 years of follow-up, 13.7% of the patients had a hospitalization or emergency department visit for heart failure, 7.1% developed stroke, 5.7% had a gastrointestinal bleeding and 3.9% had a myocardial infarction.

The overall risk of stroke is around five times higher among AF patients compared to the general population [80]. While paroxysmal AF seems to carry the same risk as permanent AF [77], the risk of stroke depends upon age, sex and concomitant risk factors [81-83]. Cardiac failure or dysfunction, hypertension, age ≥ 75 years (≥ 65 years), diabetes mellitus, previous stroke, other vascular disease and female gender have been identified as important risk factors for stroke in AF patients and are implemented in the modified CHA₂DS₂-VASC-score, that has been recommended in the decision-making about OAC treatment in order to prevent stroke in AF patients [63, 84]. The increased risks of both death and stroke are reduced by OAC [63, 66, 77, 85], but the adherence to OAC treatment has been found unsatisfactory in previous studies [86-89].

1.2.5 Etiology and risk factors

Although the understanding of the etiology of AF is still incomplete, a broad spectrum of risk factors has been associated with AF during the last decades. Recently, several papers divided these into conventional or validated risk factors that are well

documented, and less established, less validated, newer or emerging risk factors [90-92]. Risk factors for AF based on recent reviews are summarized in table 1. Endurance sport practice and endurance exercise are listed among the less established risk factors for AF.

Historically, the term lone AF has been used to describe AF in younger individuals without any other cardiovascular disease or other detectable relevant co-morbidity. However, the long list of emerging risk factors has raised the questions whether lone AF does exist, and whether the term should be avoided or not [91].

Table 1. Established and less established risk factors for atrial fibrillation, based on recent reviews^a [90-92].

Established risk factors	Less established risk factors
Advancing age	Obesity
Male gender	Body height
Hypertension	Obstructive sleep apnea syndrome
Coronary heart disease	Chronic obstructive pulmonary disease
Valvular heart disease	Chronic kidney disease
Heart failure	Subclinical hyperthyroidism
Diabetes mellitus	Excessive alcohol consumption
Hyperthyroidism	Smoking
Genetic factors	Coffee
	(Biomarkers of) inflammation (CRP, TNF-alfa, IL6)
	Biomarkers of hemodynamics stress (ANP, BNP)
	Biomarkers of cardiac damage (Troponin T)
	Prolonged endurance exercise
	Endurance sport practice
	Murmur
	Pre-clinical atherosclerosis
	Birth weight >4 kg
	Psychological determinants (stress, anger, hostility)
	Left atrial dilatation
	Left ventricular hypertrophy
	Diastolic dysfunction
	Atrial conduction delay (PR-interval)

^a The list is not necessarily exhaustive.

1.2.6 Atrial flutter

AFL is an atrial arrhythmia closely related to AF. AFL is the second most common clinically relevant arrhythmia, but its prevalence is less than one tenth of that of AF [93]. Also AFL is strongly related to increasing age, most often occurs in relation to co-morbid conditions and is associated with the same long-term consequences as AF [94]. As in AF, AFL is often characterized by an increased heart rate, but unlike AF, the heart rate is regular.

1.3 Endurance exercise, sport practice and risk of atrial fibrillation

1.3.1 Previous studies of Norwegian cross-country skiers

Already in 1978 Lie and Erikssen showed that ECG abnormalities were frequent in male Norwegian cross-country skiers participating in the Birkebeiner race [95]. After five years follow-up, they concluded that the abnormalities probably were explained by physiological adaption to exercise, and that exercise seemed to protect against CHD [96]. In the BirkOpp-study, Grimsmo, *et al*, studied morbidity and mortality in a 28-30-years follow-up of 78 of the same skiers. The skiers were aged 54-92 years at follow-up and had a high overall prevalence of AF of 16.7%. The prevalence of lone AF was 12.8 % [97]. Echocardiographic evaluation revealed that a high proportion of the skiers had enlarged left atrium dimensions. Long PQ time, bradycardia and left atrial enlargement were predictors for AF in this study [98]. The mortality was lower in the skiers compared to the general population [99]. Sivertsen, *et al*, studied 24 cross-country skiers who had been part of the Norwegian national team 25 years after their active competing period [100]. The main result of this study was that the athletes had maintained their physical capacity well after concluding their careers. Two athletes developed paroxysmal AF during the follow-up. In another study, Bjørnstad, *et al*, followed 30 Norwegian elite endurance athletes for 15 years [101]. All 30 had ended their professional careers, but were still engaged in recreational activities. There were no cases of AF, AFL or other clinical events during the follow-up.

1.3.2 Previous studies of atrial fibrillation in athletes

In 1998, Karjalainen, *et al*, were the first to describe an association between endurance sport practice and AF [8]. Finnish male elite orientation runners aged 35 to 59 years at inclusion were compared with healthy men of the same age and followed-up for ten years. Individuals with incident cardiovascular diseases during the follow-up were excluded. The prevalence of lone AF was five-fold higher in the orientation runners than in the control group (OR 5.5 (CI 1.3 – 24.4)). The main strengths of this study were the long follow-up and that also mortality and cardiovascular diseases were recorded. The study was limited by a low AF incidence and a twice as high number of drop-outs in the control group compared to the athletes. Interestingly, when analyzing the data without excluding those with incident cardiovascular diseases others than AF, there were no significant difference in the AF incidence between the groups [102]. Since 1998, atrial arrhythmias have been studied in other populations of athletes. Studies published until 2012 are summarized in table 2.

Table 2. Studies of atrial fibrillation in athletes published until 2012.

Study	Study design and population(s)	AF cases	Risk estimates	Comments
Sivertsen, 1994 [100]	Cohort study, 24 Norwegian elite cross-country skiers, 25 years follow-up, no control group	2	-	1 death due to myocardial infarction.
Karjalainen, 1998 [8]	Cohort study, 262 Finnish elite orientation runners vs. healthy recruits, 10 years follow-up	12 athletes, 2 controls	Lone AF: OR 5.5, CI 1.3 – 24.4	Higher number of drop-outs in the control group.
Molina, 2008 [103]	Retrospective cohort study, 252 Spanish non-elite marathon runners vs. sedative controls	9 runners, 2 controls	HR 8.8 (CI 1.3-61.3)	Shorter follow-up period in the control group (6 vs. 11 years). 44% smokers.
Baldesberger, 2008 [9]	Retrospective cohort study, 62 Italian former professional cyclists vs. golf players, mean follow-up 38 years	2 AF, 4 AFL, none in controls	-	71% admitted use of doping. High prevalence of CHD and hypertension
Bjørnstad, 2009 [101]	Cohort study, 30 Norwegian elite endurance athletes, no control group	None	-	
Grimsmo, 2010 [97]	Cohort study, 78 Norwegian veteran cross-country skiers, 28-30 years follow-up, no control group	13 (16.7%)	-	Prevalence of lone AF 12.8%.
Pelliccia, 2010 [104]	Cohort study, young Italian elite athletes, mean follow-up 8.6 years, no control group	None	-	Mean age 22 at inclusion.
Van Buuren, 2012 [105]	Cross-sectional study, 33 former top-level German handball players	10	-	Selection of athletes with symptoms.

AF = Atrial fibrillation. AFL = Atrial flutter. CHD = Coronary heart disease. OR = Odds ratio. HR = Hazard ratio.

A common limitation of all these studies is the low number of AF cases. Another important limitation of many studies is the inadequate controlling for confounding factors. Despite a high prevalence of smokers among the Spanish marathon runners, only age and hypertension were included in the regression model [103]. Among the Italian cyclist, 44 out of 62 reported use of amphetamine or anabolic steroids [9]. The prevalence of AF is very low in young populations, and this is the most likely explanation for the negative results of the studies conducted in young Italian and Norwegian elite athletes [100, 104].

1.3.3 Previous studies of the association between endurance exercise and the risk of atrial fibrillation

Until 2012, one study had prospectively investigated the risk of AF by endurance exercise in a larger population. In the Physicians Health Study, 16,921 healthy male doctors aged 40-84 years were followed for 12 years [106]. Both exercise and AF were self-reported by questionnaires and 1661 men reported AF during the follow-up. A modestly increased risk for AF was found among the most active physicians who reported five to seven weekly hours of exercise (aRR 1.20 (CI 1.02 – 1.41)). In subgroup analyses, the AF risk was increased only in men aged <50 years who exercised five to seven days per week, and jogging was the only type of activity associated with AF. The self-reporting of both the exposure and the outcome is the main limitation of this study. Furthermore, its generalizability is uncertain, because healthy physicians represent a selected population that might report both exercise and health outcomes differently from other populations.

A group of sports cardiologists in Barcelona has studied sport practice among patients with lone AF attending their outpatient arrhythmia clinic. Among 1160 patients consecutively referred to this clinic, 51 men aged ≤65 years with lone AF were identified. 63% of the men with lone AF were sportsmen, compared to 15% in the general Catalanian population [107]. The same 51 men were included in a case-control study and compared to 109 controls from the general population. In this analysis, current sport practice combined with >1500 lifetime hours of self-reported exercise was associated with an OR for lone AF of 2.87 (CI 1.20-6.91). The authors suggested a threshold of 1500 hours of exercise that must be exceeded to facilitate AF [108]. In a third study, the Barcelona group demonstrated that PA, body height and left atrial size predicted lone AF [109]. This prospective case-control study of 107 patients with lone AF and 107 age- and sex-matched controls is interesting because both occupational PA, exercise and sports activity were assessed using a detailed questionnaire. All activities were categorized by intensity, but unfortunately and probably due to the small study size, both occupational PA and exercise were analyzed together in the multivariable regression analysis. This implies that occupational PA of high intensity was classified together with for instance competitive sport practice. The CIs were wide and overlapping between the categories of activity and the study was not able to demonstrate a dose-response relationship. A main limitation of all three studies might be that the outpatient arrhythmia clinic in Barcelona is known for its expertise in sports cardiology, which is likely to have introduced selection bias.

1.3.4 Meta-analysis and reviews

In 2009, six case-control studies with a total of 655 athletes and 895 controls were included in a meta-analysis. The overall risk of AF was found to be significantly higher in the group of athletes than in the controls, with an OR for AF of 5.3 (CI 3.6 – 7.9) [110].

In 2012, we published a review article including both the meta-analysis and previous studies and concluded that the literature provided support for an increased risk of AF related to prolonged endurance exercise [111]. We discussed a number of important limitations: Two of the studies were based on the same patient material [107, 108], which might raise the suspicion of publication bias and an overestimation of the studied association. Most studies were likely to be affected by selection bias [8, 9, 103, 106, 108, 109, 112], and some studies had a high risk of information bias, because the registration of the endpoint could be associated with the studied exposure [108, 109]. Finally, we highlighted the lack of controlling for confounding factors in some studies [8, 106, 113].

Until 2012, several reviews were published, including largely the same studies as we did. Three reviews were published by Mont or others from the Barcelona group and concluded that growing evidence supports that prolonged endurance sport participation can cause cardiac structural changes and alterations in the autonomic system, which can facilitate atrial arrhythmias [114-116]. Sorokin, *et al*, concluded that evidence support that athletes are at increased risk of AF [117]. Turagam, *et al*, concluded that the prevalence of AF seemed to be higher in individuals involved in prolonged sport practice compared to general populations, but that evidence for a causal relation between sport practice and risk of AF was lacking [118]. On the other hand, Delise, *et al*, stated that there is no convincing data that sport itself may be the cause of AF and that a possible facilitating effect on AF is limited to vigorous endurance exercise [102]. Also Müller-Riemenschneider, *et al*, concluded that the quality of evidence for an increased risk of AF by exercise was low, and that the risk is likely to be overestimated in most studies [119].

1.3.5 Summary of previous studies

Thus, the results of a few studies indicated a high prevalence of AF in athletes and an association between endurance sport practice and an increased risk of AF. With exception from the Physicians Health Study, which was conducted in a selected population of physicians, AF risk had only been studied in relatively small samples of men. Grimsmo, *et al*, had studied prolonged endurance sport practice among Norwegian veteran cross-country skiers, but without any control group. A common limitation of all previous studies was the lack of data on the association between exercise and AF in women.

2 AIMS OF THIS THESIS

Based on the knowledge gap regarding the association between prolonged endurance sport practice and exercise and the risk of AF, the following main aims emerged for this thesis:

- I. To investigate endurance sport practice as a risk factor for AF in veteran athletes (Paper I)
- II. To investigate the association between prolonged regular endurance exercise and risk of AF in men (Paper II)
- III. To investigate the association between prolonged regular endurance exercise and risk of AF in women (Paper III)
- IV. To characterize AF and to investigate PA, endurance exercise, symptoms, drug use and subjective health among veteran cross-country skiers with AF (Paper IV)

3 MATERIALS

3.1 The Birkebeiner cross-country ski race

The Birkebeiner race has been arranged almost annually since 1932 [120]. The race was initiated to honor the rescue of the 18-months old Norwegian Prince Haakon Haakonsen in 1206. After the death of King Haakon Sverreson, the rivaling fractions the Baglers and *the Birkebeiners* were fighting to gain control over Norway. With the aim of securing the throne, a group of Birkebeiners took care of king Haakon Sverresons son Haakon and protected him against the Baglers. On their way to Trondheim, the Birkebeiners chose the strenuous route across the mountains separating Gudbrandsdalen and Østerdalen, and the two best skiers among them carried the small prince. Haakon Haakonson grew to become the king who later united Norway after 1000 years of sivil war [121]. The name Birkebeiner referred to leggings of birch bark and was given by the Baglers to describe their enemies as poor and incapable. Since the Birkebeiners proved the the Baglers to be wrong, their name was later related to strength, endurance and pride. Today the word *birkebeiner* is commonly used to describe participants of the Birkebeiner race [121].

Starting in Rena in Østerdalen and finishing in Lillehammer, the host city of the Olympic winter games of 1994, in Gudbrandsdalen, the course of the race is today 54 kilometers. With a total of about 1000 uphill altitude meters and often though weather conditions, the Birkebeiner race is among the world's most challenging cross-country ski races. All participants have to carry a backpack of at least 3.5 kg, representing the weight of prince Haakon. While 147 men completed the very first race in 1932, today the race is among the most popular sport events in Norway, and around 15,000 men and women participate every year [120].

3.2 The Birkebeiner Ageing Study

The study population of paper I is based upon 1) a cohort of male veteran cross-country skiers aged ≥ 65 who participated in the Birkebeiner Ageing Study, and 2) a cohort of men of the same age group participating in the population-based Tromsø Study.

3.2.1 The Birkebeiner Ageing Study

The Birkebeiner Ageing Study is a longitudinal study of veteran skiers participating in the Birkebeiner race. The main purpose of this study is to investigate associations between endurance sport practice and health in advanced age. Based on result lists provided by the race organizer, all 658 Norwegian skiers aged ≥ 65 years who completed the race in 2009 or 2010 and had a Norwegian postal address were invited to participate.

The inclusion of participants to the Birkebeiner Ageing Study took place in 2009 and 2010. Altogether, 484 participants in Birkebeinerrennet 2009 received a postal questionnaire together with an invitation letter during October the same year. During December, 116 individuals who had not responded to this invitation received a postal reminder. Correspondingly, 174 participants in Birkebeinerrennet 2010 who were not already included in the study received the questionnaire and invitation letter during November 2010. In total, 90 individuals were reminded by e-mail during January 2011, using e-mail addresses provided by the Birkebeiner race organizer. This, however, was not successful, as many participants were registered with the e-mail address of family members or others. Therefore, 50 individuals were also reminded by a telephone call.

Due to low number of female participants, only men were included in the analysis of this work. All male responders, 509 out of 607 invited men (84%) aged 65 to 90 years, were included. In order to investigate endurance sport practice as a risk factor for AF, cross-sectional baseline data from the Birkebeiner Ageing Study were compared with data from the sixth survey of the Tromsø Study (Tromsø 6).

3.2.2 The Tromsø Study

The Tromsø Study is a population-based general health study in the largest city in Northern Norway [122]. Since the study was initiated in 1974, repeated cross-sectional surveys have been carried out. Tromsø 6 took place in 2007-2008. In this survey, 19,762 inhabitants in Tromsø aged ≥ 30 years were invited to participate. In the age group 60-87, all inhabitants were invited. In total, 12,984 men and women participated (66%). The response rate was highest among men aged 65-69 (78%) and lowest among the oldest men aged ≥ 85 (28%) [123]. In this work, 1768 out of 2757 invited men aged 65 to 87 years (68%) were included.

3.3 The Birkebeiner Atrial Fibrillation Study

As the Birkebeiner Ageing Study was not originally designed to study AF, to further investigate the association between prolonged endurance exercise and risk of AF, a second study was designed: The Birkebeiner Atrial Fibrillation Study. The papers II, III and IV are based upon this study. Figure 2 illustrates the inclusion process of the Birkebeiner Atrial Fibrillation Study. The study population of this retrospective cohort study comprises two distinct cohorts: 1) A cohort of veteran cross-country skiers aged ≥ 53 years who had been participating in the Birkebeiner race (different from the cohort of the Birkebeiner Ageing Study), and 2) a subset of participants in the population-based Oslo Health Study.

During June 2012, all 7500 invitees in the Birkebeiner Atrial Fibrillation Study received a questionnaire together with an invitation letter. The questionnaire was identical for all participants, regardless of which cohort they were recruited from. A first reminder was sent out to 3505 non-responders during September the same year. In addition, 888 individuals who had filled out and sent in the questionnaire but not completed the consent form were reminded. A second reminder was sent out during December 2012.

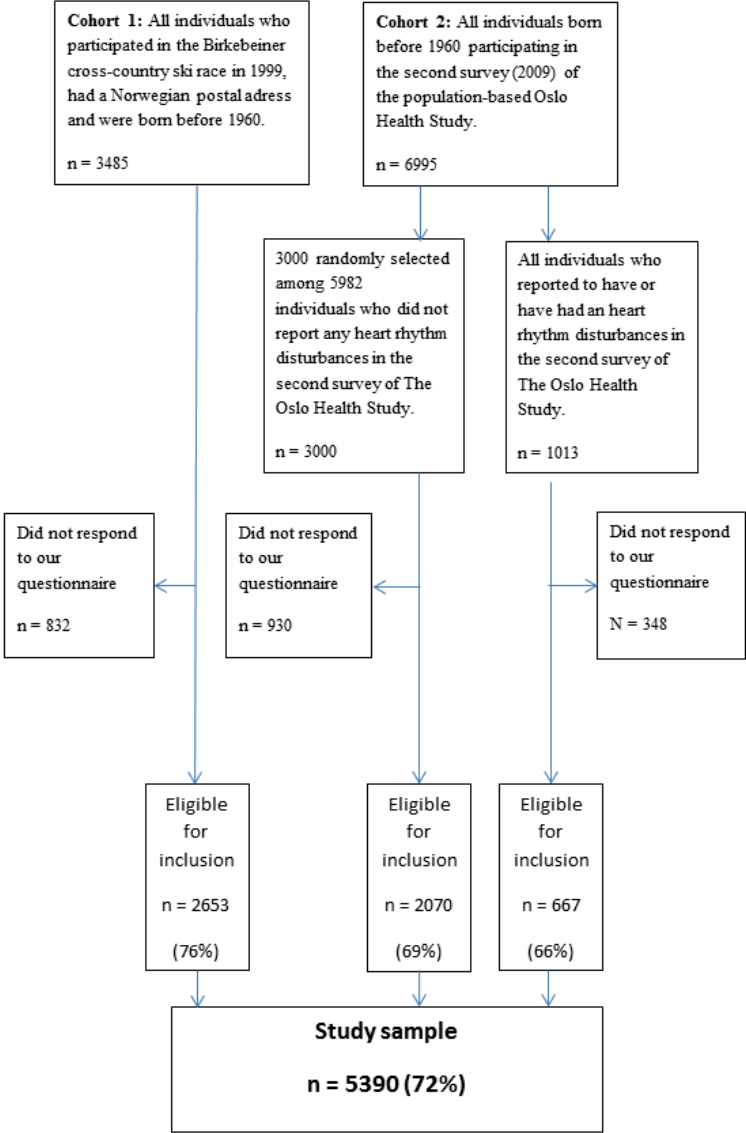
3.3.1 The cohort of veteran cross-country skiers

Based on result lists provided by the race organizer, all men and women who had participated in the Birkebeiner race in 1999, were aged ≥ 40 years at that time and had a Norwegian postal address were invited to take part in this study. Among 3485 invited skiers, 2653 (76%) responded. Among 3114 invited male skiers, 2366 (76%) men participated in the study. In total, 286 out of 371 (77%) invited female skiers took part in the study. In order to cover the range of exposure from physical inactivity to prolonged regular endurance exercise, the cohort of veteran skiers was combined with a subset from The Oslo Health Study.

3.3.2 The Oslo Health Study cohort

The Oslo Health Study was an age-stratified population-based health study [124]. Men and women aged ≥ 53 years (born in 1924, 1925, 1940, 1941, 1954 and 1955) who participated in the second survey of the Oslo Health Study in 2009 and had given consent to be re-contacted for further studies were invited to take part in the Birkebeiner Atrial Fibrillation Study. Out of 5982 individuals who had not reported heart rhythm disturbances in the 2009 survey, 3000 were randomly selected and invited to take part in the study. In addition, all 1013 individuals who had reported heart rhythm disturbances were invited, in order to maximize the number of endpoints. In total 2737 out of 4013 invited men and women from the Oslo Health Study (68%) participated in the Birkebeiner Atrial Fibrillation Study. In total, 1179 out of 1885 invited men (71%) and 1393 out of 2130 invited women (65%) responded.

Figure 2. Recruitment of participants to the Birkebeiner Atrial Fibrillation Study, based upon two distinct cohorts.



4 METHODS

The data used in the Birkebeiner Ageing Study are entirely based on information obtained by questionnaires. When designing the questionnaire to this study, we chose questions that had been used in the Tromsø Study, in order to allow comparing analyses.

The data in the Birkebeiner Atrial Fibrillation Study were mainly obtained by questionnaires, but in 416 individuals with self-reported AF, hospital medical records were reviewed in order to confirm the AF diagnoses. English translations of the questionnaires are included in the appendix of this thesis.

4.1 Assessment of the main outcome atrial fibrillation

The main outcome of the papers I, II and III was AF. AF was measured differently in the three papers: In the papers I and III, AF was self-reported by questionnaires. In paper II, AF and AFL confirmed by ECG in the review of medical records were the main outcomes, while AF that was self-reported by questionnaires was a secondary outcome. Lone AF was another secondary endpoint of paper II.

4.1.1 Self-reported atrial fibrillation

In the Birkebeiner Ageing Study, AF was defined as positive response to the question *Do you have or have you had atrial fibrillation?*

In the questionnaire of the Birkebeiner Atrial Fibrillation Study, AF was assessed with two questions: *Do you believe yourself that you have or have had atrial fibrillation?* and *Have you been diagnosed as suffering from atrial fibrillation by a doctor?* In this study, we also included questions regarding the first AF diagnosis, subtype of AF and frequency of symptoms. AFL and other supraventricular tachycardia (SVT) were not assessed in the questionnaire but registered during the review of medical records.

4.1.2 Atrial fibrillation confirmed by ECG

When available, medical records were reviewed according to a predefined protocol for subjects who reported AF in the questionnaire of the Birkebeiner Atrial Fibrillation Study, stated a Norwegian public hospital as the place where AF had been diagnosed and gave consent. Among 694 study participants with self-reported AF, 574 (83%) gave consent to the review of their medical records. 92 participants reported that AF been diagnosed by their general practitioner (GP). Initially, we tried to identify and get access to these out-of-hospital medical records. However, this turned out to be a difficult task because the cases were distributed among very many GPs across Norway and because many of the GPs lacked routines for use of patient data in research. Some of the participants had been diagnosed abroad and some did not name the hospital where AF had been diagnosed, leaving 472 who had also named a hospital. In the end, records were available for review in 416 out of these 472 (88%) individuals.

The review of medical records in 18 different hospitals took place in the period between February 1st and June 1st 2013. Incident arrhythmias (AF, AFL, other SVT,

atrioventricular block, ventricular tachycardia) up until 31.12.2012 were identified by ECGs. In cases of uncertain diagnoses, an endpoint committee consisting of two experienced cardiologists was consulted. In 19 cases where an ECG could not be found, diagnoses from the medical record text were used.

AF was classified as “lone” if the review did not reveal other relevant diseases (concomitant heart diseases, diabetes mellitus or surgery or treated infection during the past seven days before AF diagnosis). In individuals with hypertension, the arrhythmia was classified as lone only if echocardiography findings were available and normal.

4.2 Assessment of other outcomes

The endpoints of paper IV were leisure-time PA during the past year, current engagement in regular endurance exercise, palpitations, functional capacity, drug use and subjective health.

4.2.1 Leisure-time physical activity and endurance exercise

We assessed leisure-time PA during the past year using the question *State the movement and PA you engage in during your leisure time. If your activity level varies between summer and winter, note an average value. Tick the most appropriate box only.* A five-level scale was condensed into the four categories [3]: 1) Sedentary (reading, sitting still, other sedentary activity or light activities like walking, less than 4 hours per week); 2) Light PA (walking, cycling or other activity for at least 4 hours per week); 3) Moderate PA (recreational exercise, heavy gardening, for at least 4 hours per week); and 4) High PA (Regular hard exercise or competitive sports several times per week).

We specifically defined endurance exercise in the questionnaire as regular endurance exercise for at least 30 minutes at least three times per week with the purpose of increasing physical endurance capacity. The endpoint regular endurance exercise in paper IV was defined as positive response to the question *Do you still engage in regular endurance exercise?*

4.2.2 Symptoms, drug use and subjective health

Palpitations during the past year were assessed with the question *Have you noticed sudden changes in your heart rate or heart rhythm in the past year?*

We used the NYHA functional classification (class I-IV) in order to assess functional capacity [125], and asked the participants to report how their heart disease impacts on their functional capacity (*If you have a heart disease, how does it impact on your ability to function?*) with four answer categories: I) No limitations. Ordinary PA does not cause undue fatigue, dyspnea or chest pain, II) Slight limitations of PA, but comfortable at rest. Ordinary PA results in fatigue, dyspnea or chest pain, III) Marked limitations of PA, but comfortable at rest. Even light PA causes fatigue, dyspnea or chest pain, and IV) Inability to carry out any PA without discomfort. Fatigue or chest pain may be present even at rest.

Drug use related to AF was assessed with the question *Do you use the following medicines as a result of atrial fibrillation?* with the following possible answers: Beta-blockers (e.g. Selo-Zok, Metoprolol, Sotalol, Sotacor, Emconcor), calcium-blockers (e.g. Isoptin, Verapamil, Veracard), amiodarone (Cordarone), flecainid (Tambocor), Digitoxin, digoxin (Lanoxin), acetylsalicylic acid (Albyl-E, Magnyl-E), dronedarone (Multaq), warfarin (Marevan) and dabigatran (Pradaxa).

Finally, we assessed subjective health with the question *How do you rate your own health?* with four answer categories (Poor, fair, good and very good) [126].

4.3 Assessment of the main exposure endurance exercise

Under the assumption that participation in a long-distance cross-country ski race when aged ≥ 65 years requires regular endurance exercise, *endurance sport practice* in the Birkebeiner Ageing Study was defined as belonging to the cohort of veteran cross-country skiers.

In the Birkebeiner Atrial Fibrillation Study, endurance exercise was specifically defined in the questionnaire as regular endurance exercise for ≥ 30 minutes at least three times per week with the purpose of increasing physical endurance capacity. The first question regarding endurance exercise used in the questionnaire, was *Have you ever been practicing regular endurance exercise?* (yes/no). Thereafter, the participants were asked to report the cumulative number of years they had been exercising regularly on an eight-level scale: Never, <5, 5-9, 10-19, 20-29, 30-39, 40-49, 50-59, ≥ 60 years. In paper II, the scale was condensed from eight into five categories with cut-off at 40 years of exercise. In paper III, the scale was condensed into only four categories due to the lower number of women exposed to exercise in the study. Participants who had not answered any of these two questions were assumed not to have been exercising regularly and given the value Never.

4.4 Covariates

All covariates were self-reported by questionnaires. Diseases were assessed with the question *Do you have or have you had (name of the disease)?* In addition to age, gender, height and weight, we assessed the following established AF risk factors in the questionnaires of both the Birkebeiner Ageing Study and the Birkebeiner Atrial Fibrillation Study: Concomitant heart diseases (myocardial infarction, angina pectoris, heart valve pathology and heart surgery), hypertension, diabetes mellitus and hyperthyroidism. We also assessed the following less established risk factors and other possible confounding factors in both studies: Lipid-lowering treatment, stroke, use of tobacco and alcohol, education and marital status. We calculated BMI based on self-

reported height and weight. In paper IV, we estimated CHA₂DS₂-VASc score using age, sex and self-reported CHD, hypertension, stroke and diabetes mellitus [84].

We used direct acyclic graphs (DAGs) to identify covariates appropriate for adjustment in all regression analyses. DAGs are causal graphs that summarize all relevant causal relations between an exposure and an outcome, and is a tool in the analysis of causal associations [127]. Causal graphs do not prove causality, but are based upon causal thinking and define a main exposure and a main outcome. In DAGs, covariates are defined as confounders, mediators or colliders. In the regression analyses, adjustments are made for confounders, but not for colliders. Mediators are adjusted for when aiming to estimate the direct effect between exposure and outcome.

4.5 Statistical analyses

Although having observed a higher AF prevalence in the Birkebeiner Ageing Study, we assumed a prevalence of 5% in the power calculation of the Birkebeiner Atrial Fibrillation Study, due to a lower expected mean age of this study population. In order to find an OR of 1.5 with a 95% CI with a power of 80%, in a study where 50% were exposed to exercise and the prevalence of AF was 5%, around 5000 subjects were required.

We used Student's t-test for means of continuous variables and Pearson's Chi square of independence for categorical variables to compare characteristics of the study participants. In paper I, a linear regression analysis was used to calculate crude (cRDs) and aRDs with CIs and a logistic regression analysis was used to calculate the aOR with CI. In paper II, III and IV, aORs with CIs were calculated by logistic regression analyses. We tested all relevant covariates, but included only established risk factors and covariates changing the estimates with $\geq 10\%$ in the final models.

In paper II and III, we adjusted for different selection probabilities by using inverse probability weighting: Study participants who were invited because they had previously participated in the Birkebeiner race or because they had previously reported arrhythmias in The Oslo Health Study were weighted by one (all eligible individuals were invited). Participants who were randomly selected among participants in the Oslo Health Study were weighted by two (3000 out of 5982 were invited). Due to the different selection probability, we reported the weighted prevalence for the participants in the Oslo Health Study in paper II, and weighting was used in all regression analyses of paper II and III.

In the papers II and III, we excluded study participants who had been invited because they had reported heart rhythm disturbances in the Oslo Health Study but turned out not to have any arrhythmias. In paper III, we excluded women aged >75 years in order to reduce recall bias. In order to increase the comparability between the AF subpopulations of the study, we excluded individuals aged >85 years in paper IV. Due to the strong positive relation between age and risk of AF, we performed sensitivity

analyses after exclusion of men aged >75 years to explore the influence of age distribution on the risk estimates in paper II. In addition, sensitivity analyses after exclusion of men diagnosed with arrhythmia before the age of 40, men invited because they had previously reported heart rhythm disturbances and men with self-reported AF but unavailable medical records were conducted. In paper II we reported estimates for the two distinct cohorts (Birkebeiner skiers and participants from the Oslo Health Study) separately and for the whole study sample.

All statistical analyses were conducted using SPSS version 20.0 (IBM, Armonk, New York, USA) or STATA version 12.1 (StataCorp LP, Lakeway Drive, Texas, USA).

4.6 Ethical considerations

The studies in this thesis were approved by the Regional Committee for Medical and Health Research Ethics (REK) and comply with the Declaration of Helsinki. Together with the questionnaires, all invitees received invitation letters that had been approved by REK. Informed written consents to participate in the study were obtained. The review of medical records was only performed for participants who had actively given a written informed consent to the review. Approvals for the review of medical records were obtained from the responsible authorities for research and data protection for each hospital reported by at least one participant. Inclusion in the studies was considered not to have any harmful effects for the participants.

5 RESULTS

5.1 Paper I: Endurance sport practice as a risk factor for atrial fibrillation

Title: Increased risk of atrial fibrillation among elderly Norwegian men with a history of long-term endurance sport practice

Compared to men of the same age from the general population of Tromsø, veteran cross-country skiers aged ≥65 years (mean age 69, range 65-90 years) had a low prevalence of the established AF risk factors CHD, hypertension and diabetes mellitus. The crude prevalence of AF was 13.2% in the veteran athletes and 11.6% in the general population. The prevalence of AF after exclusion of persons with CHD was 13.0% in the veteran athletes and 9.8% in the general population. After multivariable adjustment for age, height, BMI, CHD, hypertension, diabetes mellitus, smoking, alcohol consumption, leisure-time PA during the past year and education, endurance sport practice gave an added risk of AF of 6 pp (aRD 6.0 (CI 0.8-11.1)), corresponding to an aOR of 1.90 (CI 1.14-3.18). The risk of AF increased with 0.4 pp per added year of age and with 0.3 and 0.6 pp per cm of height and unit of BMI added, respectively. Also hypertension and CHD were significantly associated with an added risk for AF.

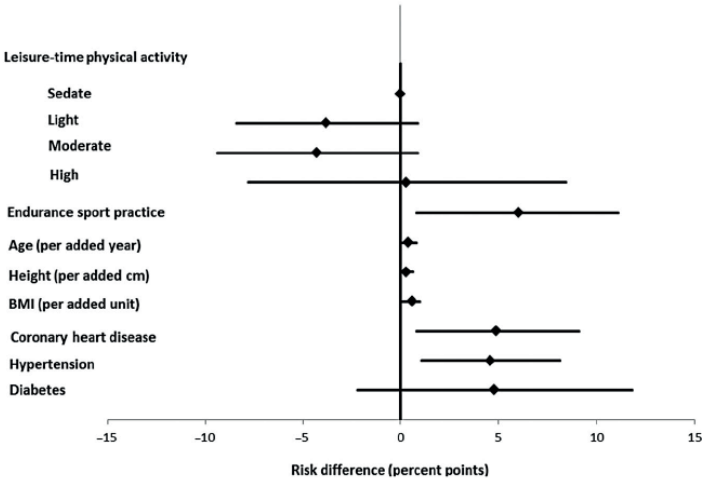


Fig. 2. Studied risk factors for atrial fibrillation. Estimated atrial fibrillation risk differences with 95% confidence intervals by selected covariates. Both study populations analyzed together, men 65-90 years old.

5.2 Paper II: Years of regular endurance exercise was associated with a graded increased risk of atrial arrhythmias in men

Title: Effect of years of endurance exercise on risk of atrial fibrillation and atrial flutter

The prevalence of self-reported AF was 12.5% among the veteran cross-country skiers (mean age 66, range 53-92 years) and the weighted prevalence among the participants in the Oslo Health Study was 10.3%. While AF was confirmed by ECG in 219 out of 306 men (72%) with self-reported AF and available medical records, 52 (17%) had AFL. After multivariable adjustment for age, height, concomitant heart disease, hypertension, diabetes mellitus and cohort affiliation, cumulative years of regular endurance exercise were associated with a gradually increased risk of AF with an aOR for AF of 1.16 (CI 1.06-1.28) per ten years of exercise, 1.16 (CI 1.00-1.36) among the skiers and 1.20 (CI 1.06-1.35) among the men from the Oslo Health Study. Regular endurance exercise was also associated with a gradually increased risk of AFL. The aOR for AFL per ten years of exercise was 1.42 (CI 1.20 – 1.69) and did not differ between the two cohorts. The aORs per ten years of exercise were 1.26 (CI 1.10 to 1.44) for lone AF and 1.12 (CI 1.04-1.19) for self-reported AF.

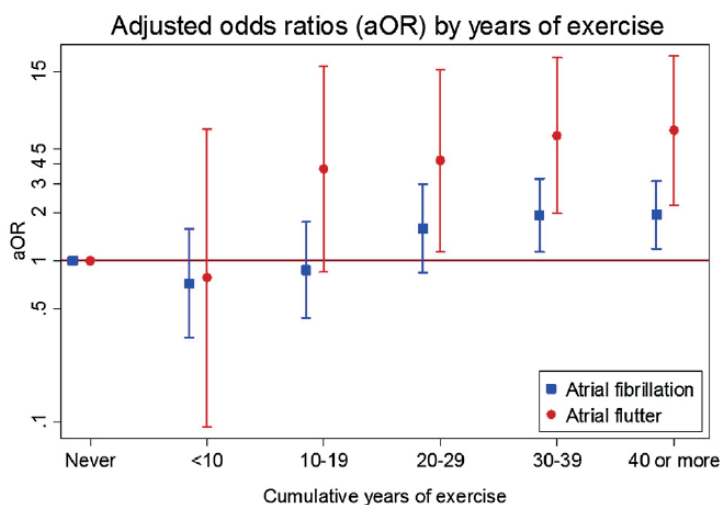


Figure 2. Adjusted odds ratios with 95% CIs for AF (n = 219) and atrial flutter (n = 52) by categories of exercise years, men aged 53 to 92 years (n = 3,545). Adjusted for age, height, heart disease, hypertension, diabetes mellitus, high-intensity exercise during the previous 12 months, and cohort affiliation.

5.3 Paper III: Prolonged endurance exercise might be associated with atrial fibrillation in women

Title: Does endurance exercise cause atrial fibrillation in women?

In total, 110 out of 1449 women reported AF. The prevalence of self-reported AF among female veteran cross-country skiers (n=278, mean age 62, range 53-75 years) was 8%. While 815 women had never exercised regularly, 634 had exercised regularly at some point of life, 89 of them for ≥ 40 years. Women who had never exercised regularly were older compared to women who had exercised at some point of life. Women who had exercised ≥ 20 years had a lower mean BMI and less hypertension and lipid-lowering treatment than women who had exercised < 20 years. After multivariable adjustment for age, BMI, concomitant heart disease, hypertension, diabetes mellitus and cohort affiliation, women who had exercised for ≥ 40 years seemed to have an increased risk of AF of borderline significance (aOR 2.18 (CI 0.94-5.06)) compared to women who had never exercised regularly.

5.4 Paper IV: The majority of veteran athletes still engaged in regular physical activity and exercise after the onset of atrial fibrillation

Title: Physical activity, symptoms, medication and subjective health among veteran endurance athletes with atrial fibrillation

AF was reported by 322, medical records were available for review for 177 and AF was confirmed in 140 veteran cross-country skiers. Among the study participants from the general population, AF was confirmed in 118 cases. Among veteran skiers, 52% had paroxysmal AF, 23% had persistent AF and 24% had permanent AF, while the corresponding proportions in the general population were 52%, 17% and 30%. Veteran athletes with AF were older and had a higher prevalence of co-morbid conditions than veteran athletes without AF, but were younger and had a lower BMI and less co-morbidity than their counterparts with AF in the general population. Only 11% of the veteran skiers with AF were inactive, 70% reported moderate or high PA during the past year and 64% still engaged in regular endurance exercise. After multivariable adjustment for age, sex, BMI, co-morbid conditions and number of completed Birkebeiner races, AF was associated with poor subjective health among veteran athletes (aOR 2.8 (CI 1.7-4.6)). Almost two out of three reported palpitations during the past year and one out of three had experienced reduced functional capacity, but symptoms did not differ significantly between the veteran athletes with AF and the general AF population, between AF subtypes or between AF with and without co-morbid conditions. One out of three with AF and an estimated CHA₂DS₂-VASc-score ≥ 2 was not treated with OAC.

6 DISCUSSION

The results of this thesis support that endurance sport practice might be a risk factor for AF in men aged ≥ 65 years, suggest a graded positive association between years of regular endurance exercise and risk of atrial arrhythmias in men, and indicate that prolonged endurance exercise might be associated with an increased risk of AF also in women. In addition, it has been demonstrated that the majority of veteran athletes remains physically active and engage in regular endurance exercise even after the onset of AF. The study populations, including veteran athletes that on average have been exposed to regular endurance exercise and sport practice for very many years, confirmation of AF diagnoses during a review of medical records, very high attendance rates and the collection of a broad specter of possible confounding factors, are main strengths of these studies. Some important issues related to the study design, exposure and outcome measurements and confounding, however, will be discussed.

6.1 Methodological considerations

The observational design of the studies of this thesis has some important limitations. Observational studies can be hampered by selection bias, information bias and confounding. Furthermore, the design does not allow any conclusions about a causal relationship.

6.1.1 Study design

To conduct a randomized controlled trial in order to investigate the relation between prolonged endurance exercise and risk of AF, might seem unfeasible and would also have carried some ethical problems. Study participants would have to be followed prospectively for a long time, with high risk of drop-outs and problems with competing risk. Therefore, a retrospective study design appeared to be the most feasible in order to study this association. As it might be assumed that participation in the Birkebeiner race requires regular endurance exercise, the use of participation lists from the race organizer provides some objective information on the exposure, in addition to the retrospective self-reporting of exercise.

In paper I, we used cross-sectional data from the Birkebeiner Ageing Study and the Tromsø Study. The main exposure was participation in the Birkebeiner race and the main outcome was self-reported AF. This study design might be affected by selection bias, because participation in the study might be associated with both the exposure and the endpoint: Individuals who had discontinued their endurance sport practice due to AF (or other diseases) did not have the opportunity to participate in the study. This “healthy exerciser effect” might have caused an underestimation of the AF prevalence among the veteran skiers and the AF risk estimates.

Also in the Birkebeiner Atrial Fibrillation Study, we used cross-sectional data. In this study, however, the study population was based upon a cohort of veteran skiers that had

been participating in the Birkebeiner race many years earlier (1999) and the study might be characterized as a retrospective cohort study [128]. Because AF is uncommon before the age of 40 and all skiers who were aged ≥ 40 in 1999 were invited, the results of this study are less likely to be affected by a “healthy exerciser effect”. On the other hand, individuals with AF who had been exposed to endurance exercise might have been more prone to participate in the study, and this possible selection bias might have caused an overestimation of the risk estimates. However, as high attendance indicates that the study population gives satisfactory information about the target population [129], the risk of an overrepresentation of AF cases is reduced by the high attendance rate in the study. Even in studies with much lower attendance rates, it has been demonstrated that effect estimates are not necessarily biased by under- or overrepresentation of the exposure [130, 131].

While inadequate control groups and the lack of a reference point in the general population have been pointed out as a weakness of previous studies [111, 132], in the Birkebeiner Atrial Fibrillation Study we combined two distinct cohorts with the aim to cover the whole range of exposure from physical inactivity to prolonged endurance exercise. The combination of two cohorts that differ in many aspects might be questioned, because unmeasured confounding like psychosocial factors and a family history of cardiovascular diseases could influence the risk of AF [133, 134]. However, the association between years of exercise and risk of AF was consistent also when the two cohorts were analyzed separately (paper II).

The low number of female participants confines the possible gender perspectives of the Birkebeiner study populations. Female response rates were at the same level as in men, but the low proportions of women participating in our studies reflect that women represent a minority among veteran athletes participating in long-distance cross-country ski races.

6.1.2 Atrial fibrillation measurements

AF studies are limited by the natural course of the disease. Firstly, 30-40% of the individuals with AF might be asymptomatic [135-137]. Secondly, in individuals with paroxysmal AF, the arrhythmia can only be diagnosed with certainty during an attack. Thus, AF studies are likely to have high rates of AF cases that are misclassified as without arrhythmia (low sensitivity). The proportion of persons with undiagnosed AF might be especially high in our study populations, as old people often have less symptomatic AF than younger [137-139]. Self-reported AF was the main endpoint in paper I and paper III. As demonstrated in figure 1, the prevalence of AF was higher in Tromsø 6, where AF was self-reported, compared to other prevalence studies. High sensitivity might be an advantage of self-reporting of AF, as also undiagnosed cases are counted, but a limitation of our studies is that we did not investigate the sensitivity of the AF measures.

A key question is whether the misclassification is differential and associated with the exposure. Physically inactive individuals might be less likely to experience AF symptoms [137], and active individuals might recognize symptoms earlier inactive individuals. This might have caused an overestimation of the associations between exercise and sport practice and AF. On the other hand, athletes more often have typical vagal AF with lower heart rates and paroxysms during night [118, 140], and might be more prone to ignore

symptoms. Athletes also more often have paroxysmal AF that might be more challenging to diagnose [118], and this might have caused an underestimation of the studied association.

A strength of the Birkebeiner Atrial Fibrillation Study is that AF diagnoses were confirmed in a review of medical records. Table 3 shows confirmed arrhythmias according to the two questions used in the questionnaire of the Birkebeiner Atrial Fibrillation Study. Among participants with self-reported AF, the diagnosis was confirmed in three out of four, while around 16% had other arrhythmias. In 11% the review did not reveal any arrhythmia. The positive predictive value (PPV) of a positive response to the question *Do you believe yourself that you have or have had atrial fibrillation?* was 73% for AF, but 81% when AF and AFL were analyzed together. The PPV was lowest in the subgroup that was unexposed to regular endurance exercise. This indicates that AF might be overestimated in the reference group and that the association between exercise and self-reported AF might be underestimated. The PPV did not differ largely between the two questions *Do you believe yourself that you have or have had atrial fibrillation?* and *Have you been diagnosed as suffering from atrial fibrillation by a doctor?* However, we assumed a higher sensitivity for the first question and chose to use positive response to this question as an endpoint in the papers of this thesis.

AF and AFL confirmed by ECG were the main outcomes in paper II. Medical records were available for 60% of the individuals with self-reported AF. The proportion with available records among those with self-reported AF did not differ between skiers and non-skiers, but were slightly higher in individuals who reported ≥ 30 years of regular exercise compared to the other groups of exposure. This might have caused an overestimation of the risk estimates in the highest categories of exercise. On the other hand, non-athletes have higher prevalence of co-morbid conditions and the individuals with the lowest exposure to exercise might therefore have been more likely to be hospitalized for any reason. Because AF diagnoses were confirmed using in-hospital medical records, the association between exercise and AF might be underestimated.

Table 3: Proportions with arrhythmias confirmed in the review of medical records (positive predictive values) among individuals with self-reported atrial fibrillation according to the two different question used in the Birkebeiner Atrial Fibrillation Study (n=416).

	n ^a	Results of the review, numbers and proportions (%)				
		No arrhythmia	Atrial fibrillation	Atrial flutter	Other SVT ^b	Other arrhythmias
Do you believe yourself that you have or have had atrial fibrillation?	351	40 11.4	255 72.6	28 8.0	21 6.0	7 2.0
Have you been diagnosed as suffering from atrial fibrillation by a doctor?	365	39 10.7	270 74.0	29 7.9	20 5.5	7 2.0

^a Number of review medical records among study participants who answered this question positively, gave consent to the review and named a Norwegian hospital where atrial fibrillation had been diagnosed.

^b Supraventricular tachycardia

While most previous studies have not differentiated between AF and AFL [8, 9, 141], the differentiation between these two atrial arrhythmias is an asset of our study. Subjective distinguishing between AF and AFL, however, can be difficult and AFL was not assessed in the questionnaire. Individuals who knew that they had been diagnosed with AFL and not AF might have answered “no” on the questions regarding AF, leading to an underestimation of the AFL risk estimates.

While some previous studies have used hospitalization recorded with ICD-10-codes in national in-patient registers [142, 143], others have used self-reported AF and obtained medical records for confirmation of the diagnosis [106, 144]. In order to isolate lone AF, prescription of flecainid and sotalol recorded from the Norwegian prescription registry was used as a surrogate measure for lone AF in one study [145]. All measures have limitations and comparison of results between studies is difficult. Even in studies where AF has been diagnosed using the gold standard ECG [103, 108, 109], false negative rates have not been assessed and the overall validity is therefore unknown. The results of the Birkebeiner Atrial Fibrillation Study are strengthened by the consistency between the various AF measures used in the study.

6.1.3 Measurements of other endpoints

A limitation of our studies is that we did not assess other symptoms than palpitations and functional capacity. Palpitations are, however, the most commonly reported among AF-related symptoms [72], and might be more specific than for example dyspnea. The NYHA-classification measures the physical functional capacity and was originally developed for use in heart failure patients, but has also been validated in AF patients

[72, 125]. It assesses functional capacity related to fatigue, shortness of breath or chest pain, and therefore gives some information also about these AF-related symptoms.

Self-reports of OAC use might provide imprecise information on adherence [87]. Furthermore, the Birkebeiner Atrial Fibrillation Study do not provide information on the use of novel OACs because these were not in routinely use in Norway at the time of the study [146].

Self-rated health is a reliable and valid measure of subjective overall health status, including biological, psychological and social dimensions of health, and is associated with morbidity and mortality [126, 147, 148]. It has also been used previously in studies of AF patients [73].

6.1.4 Measurement of endurance exercise

In paper II and III, we aimed to investigate a dose-response relationship in the association between endurance exercise and risk of AF and designed our own questions and scales in order to assess prolonged endurance exercise. We used an eight-level scale with a cut-off at 60 years of exercise. Thus, at least partly, the exposure occurred many decades ago and might have been difficult to recall accurately. Furthermore, the results might have been affected with recall bias: Participants with AF might have been more prone to over-report previous exercise than individuals without AF, causing a differential misclassification that could have influenced the effect estimates positively.

6.1.5 Measurement of co-morbid conditions and confounding

Confounders are variables that are associated both with the exposure and the outcome [128]. While the results of previous studies investigating the risk of AF by endurance sport practice have been questioned because many of the participants have been exposed to possible confounding factors [102, 103], the prevalence smoking and co-morbid conditions was relatively low in our studies. Furthermore, the assessment of a broad specter of AF risk factors, co-morbid conditions and other possible confounding factors is an asset of both the Birkebeiner Ageing Study and the Birkebeiner Atrial Fibrillation Study. Although self-reporting might be affected by recall bias, previous studies suggest an acceptable validity of self-reported data on diseases like CHD, hypertension [149], diabetes mellitus and stroke [150], and smoking [151].

In paper IV, we estimated CHA₂DS₂-VASc scores based on age, sex and self-reported CHD, hypertension, stroke and diabetes mellitus [84]. Congestive heart failure and vascular diseases others than CHD were not assessed in our questionnaire. This method provides only rough estimates for stroke risk, but was useful in order to assess the use of OAC in AF patients with concomitant stroke risk factors.

6.2 Discussion of the main results

6.2.1 Endurance sport practice as a risk factor for atrial fibrillation

In the Birkebeiner Ageing Study (paper I), we demonstrated a high prevalence of AF of 13.2% among male veteran cross-country skiers. This is in concordance with a previous study of veteran Birkebeiner skiers, where the prevalence of AF was 16.7%. [97]. A

higher prevalence of concomitant cardiovascular risk factors and diseases in the previous study might, at least partly explain the difference between the studies [99].

Endurance sport practice, defined as participation in the Birkebeiner race, seemed to be a risk factor for AF among men aged ≥ 65 years. This result is in line with those from previous studies conducted in younger male elite orientation runners, former professional cyclists and non-elite marathon runners [8, 9, 103]. The result is also supported by the results of a recent study by Andersen, et al, conducted among Swedish participants in the 90-kilometer cross-country ski race Vasaloppet. In this study, men who had completed \geq three races had a significant higher risk of AF, with an adjusted hazard ratio (HR) of 1.27 (CI 1.02–1.57) compared with participants who had only completed one race [142]. A main limitation of this study was the lack of a reference point in the general population [132]. The aRD estimated in the Birkebeiner Ageing Study corresponds to an aOR for AF of 1.90 (CI 1.14–3.18). This is close to the risk estimate (pooled RR for AF 1.98 (CI 1.00–3.94)) reported in a recent meta-analysis that included almost 2,000 endurance athletes of different ages [152].

In a previous study conducted among men and women aged ≥ 65 years in the United States, leisure-time PA seemed to reduce the incidence of AF in a graded manner [112]. The most active group in this study, however, had an average activity level corresponding to 1840 kcal/week, which is likely to be far below that of the majority of Birkebeiner skiers. Our results are also in contrast with the Physician's Health Study, where no association between endurance exercise and risk of AF was found among male physicians aged >50 years. The authors of this paper suggest an underestimation of the AF risk due to a "healthy exerciser effect", or that older individuals exercise less vigorously than younger [106]. The stronger exposure to exercise in the Birkebeiner Ageing Study increases its power to detect an association between exercise and AF and is likely to explain the controversial results between ours and these previous studies.

In a recently published study of cyclists in New Zealand, no association was found between participation in a bicycle race and hospital admissions due to AF when compared to the general population [153]. In this study, the majority of participants were aged <50 years, only 66 cases of AF were registered and the study might therefore not have had enough power to detect an association. In an analysis derived from two large prospective studies of walkers and runners, cardiac arrhythmias were not related to walking or running intensity or to marathon participation or performance [154]. This study, however, did not differentiate between arrhythmias.

6.2.2 Prolonged endurance exercise and risk of atrial fibrillation

In the Birkebeiner Atrial Fibrillation Study (paper II), we demonstrated a gradually increased risk of AF by cumulative years of regular endurance exercise in men. A population-based cohort study published in 2014 supports a dose-response relationship between exercise and the risk of AF. More than 44,000 Swedish men aged 45–79 were included in this study, where weekly hours of exercise at age 30 were associated with an increased risk of AF later in life. Similar to in our study, the risk of AF seemed to increase gradually, but was not statistically significant until the highest level of exercise (>5 hours exercise/week) [143]. The main strengths of this study were that it was conducted in a large cohort representing the general Swedish male population and had a high number of endpoints.

Elousa, *et al*, have suggested a threshold of 1500 lifetime hours of exercise for the development of AF [108]. However, as elite athletes in endurance sports might exercise around 1000 hours a year, and many non-elite athletes exercise 300-500 hours [155], a very high prevalence of AF should be expected with this estimated threshold. In contrast, Bjørnstad, *et al*, found no cases of AF in a follow-up study of Norwegian former elite athletes [101]. The result of paper II supports a gradually increased risk by amount of exercise rather than a threshold beyond where the risk of AF is increased. The AF risk was not statistically significantly increased until ≥ 30 years of exercise, but this might be due to lack of power of the study. Furthermore, in the light of individually different risk profiles, to set an absolute threshold seems unreliable.

Few previous studies have differentiated between AF and AFL [116]. In our study, 13% of the male veteran athletes with confirmed AF also had AFL. Among the Finnish orientation runners studied by Karjalainen, *et al*, 25% had AFL in addition to AF [8]. In a study of Italian former professional cyclists, AFL was more common than AF [9]. The result of a retrospective case-control study including 61 Belgian patients with lone AFL suggested that a history of endurance sport practice may be a risk factor for AFL [156]. While these previous studies have not estimated the risk of AFL by endurance exercise, cumulative years of regular endurance exercise was associated with a graded increased risk of both AF and AFL in the Birkebeiner Atrial Fibrillation Study. This result suggests that the dose of endurance exercise might play a role in the pathophysiology of both arrhythmias.

Despite a few negative studies and scepticism among some authors [102, 152, 157], others conclude that there is enough evidence to suggest a causal association between endurance sport practice and an increased risk of AF [116, 158-161]. However, many questions remain unanswered regarding the duration, amount, intensity and type of exercise that might increase the risk of AF [159].

6.2.3 Prolonged endurance exercise and risk of atrial fibrillation in women

Furthermore, the lack of data pertaining to women is a limitation of all previous studies [7, 118, 132]. In the Birkebeiner Atrial Fibrillation Study we investigated the association between endurance exercise and risk of AF in both genders. Although limited by weak power, the result of paper III indicates that prolonged endurance exercise might be related to an increased risk of AF also in women.

The lack of an association between endurance exercise and sport practice and risk of AF in women in previous studies might either have epidemiological explanations or be due to real gender differences. As demonstrated in figure 1, women experience AF five to ten years later than men, and low numbers of AF cases in previous studies might at least partly explain why no association has been demonstrated between exercise and AF in women previously. This is illustrated by the study of participants in Vasaloppet, where only 12 cases of AF occurred during >50,000 person-years of follow-up among women [142]. The INTERHEART-study showed that also CHD occurs later in women than in men [69]. In the Birkebeiner Atrial Fibrillation Study, women were younger and had lower prevalence of CHD, hypertension and diabetes than men, and lower prevalence of established AF risk factors is likely to be part of the explanation.

Also gender differences in the exposure to endurance sport practice might play a role. The low proportions of women among the veteran skiers in our studies (7.8% in the Birkebeiner Ageing Study and 10.6% in the Birkebeiner Atrial Fibrillation Study) demonstrate that women are less likely to participate in endurance sports events. This is supported by the results of a study conducted among Danish people who exercised regularly, where only 22% of the women compared to 37% of the men had participated in endurance sports competitions [162]. In the same study, 5% of the women compared to 10% of the men exercised >10 hours per week. In a study of Danish runners, 18% of the women compared to 34% of the men reported an average weekly running distance of >30 kilometres, while 2.5% and 10.1% reported a distance of >50 kilometres [163].

Finally, physiological gender differences might be part of the explanation. Women have physiological smaller hearts and higher heart rates, and low heart rates seem to predict AF only in men [145, 164]. Atrial morphological and functional changes have been demonstrated in female athletes [165], but in a recent study, female veteran athletes had less pronounced remodeling, lower sympathetic tone and lower blood pressure than their male counterparts [166]. The interplay between endurance exercise, sex hormones release and electrophysiological gender differences remains an unexplored field.

6.2.4 Characteristics of atrial fibrillation in veteran athletes

Paroxysmal lone AF in middle-aged men exposed to prolonged endurance exercise has previously been characterized as the typical clinical profile of exercise-related AF [116]. In the Birkebeiner Atrial Fibrillation Study of male skiers with a mean age of 69 years, 24% had permanent AF and 43% had co-morbid conditions, indicating that veteran athletes with AF represent a more heterogeneous subpopulation.

The clinical presentation of AF might vary between AF subtypes and between men and women, and is influenced by age, co-morbidity and socioeconomic status [72]. Furthermore, the lack of standardized outcome parameters in many AF studies limits the possibility of comparison between studies [135]. Palpitations and reduced functional capacity were less frequent both in veteran skiers and in the general AF population in the Birkebeiner Atrial Fibrillation Study than in previous studies conducted in general AF populations [74, 167]. While 60% had symptoms that required termination of sport activity in a study of 30 Dutch athletic men with paroxysmal AF [141], the high proportion engaging in exercise also after the onset of AF in our study supports that many individuals with AF have relatively mild symptoms [137]. Still, AF was associated with poor subjective health among veteran skiers. While this association was robust also after adjustment for co-morbid conditions in a previous study [73], subjective health seemed to depend on co-morbidity in the Birkebeiner Atrial Fibrillation Study.

Both among the skiers and in the general population in the Birkebeiner Atrial Fibrillation Study, two out of three with AF and an estimated CHA₂DS₂-VASc score ≥ 2 used OAC. Although the CHA₂DS₂-VASc score is roughly estimated in this study and self-reporting might provide imprecise information on treatment adherence [87], the result might indicate a lower OAC use in our study populations compared to other general AF populations [168]. In general, veteran athletes might be less prone to any drug treatment [118], but there are no data to support not to treat veteran athletes with AF and a CHA₂DS₂-VASc score ≥ 2 with OAC in order to prevent stroke.

The proportion using rate-controlling drugs was lower in the veteran skiers with AF compared to the general AF population in our study. This might be due to lower heart rates in athletes, or because athletes refuse to use treatment that might reduce sports performance [118]. On the other hand, the proportion using rate-controlling drugs was higher than in a previous study conducted in France during the 1990's [169]. This might reflect differences in symptom burden, co-morbidity and general health status or in AF medication prescription between countries and over time.

6.2.5 Physical activity and endurance exercise in veteran athletes with atrial fibrillation

Almost 90% of the veteran athletes were physically active also after the onset of AF, and two out of three still engaged in regular endurance exercise. Importantly, this demonstrates that veteran athletes continue to profit from the benefits of PA and exercise also after the onset of AF. In a short term, regular exercise might reduce resting heart-rates and symptoms and improve heart rate variability, exercise capacity, the ability to carry out activities of daily living and health-related quality of life in persons with AF [170-172]. In the long term, also individuals with AF can profit from the universal benefits of regular PA and exercise in terms of reduced mortality and morbidity [40].

6.2.6 General discussion

The exposure to PA or exercise varies largely and might explain the controversial results between studies. While large prospective cohort studies have typically investigated the risk of AF by self-reported PA [112, 113, 144], case-control and cohort studies with smaller sample sizes have been conducted in different populations of athletes [8, 9, 103]. The term "athlete" refers to individuals engaging in regular sport practice, but there is a wide gap between recreational exercise and elite level competitive sports, and a clear-cut definition has not existed. Furthermore, physiological adaptations to endurance exercise might differ between individuals engaged in PA and athletes exposed to prolonged regular endurance exercise, and a threshold between physiological and pathological adaptations has not been established [7].

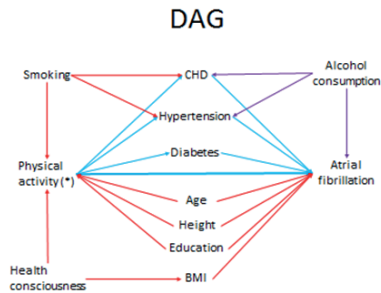
The results of paper I indicate that light or moderate PA during the past year might reduce the risk of AF. This result was not significant in our study, but is supported by the results of a Swedish study that demonstrated a reduced risk of AF by amount of PA among men with a mean age of 60 years [143], and those from the Cardiovascular Health Study (90), where self-reported PA was associated AF in a U-shaped manner in men and women aged ≥ 65 years. While moderate intensity was associated with lower incidence of AF (HR 0.72, CI 0.58-0.89), those who reported the highest activity level had the same AF incidence as the inactive individuals. Two studies that investigated the association between PA and risk of AF in women exclusively, demonstrated that higher levels of PA were associated with a lower prevalence of AF [144, 173]. In contrast, two recent meta-analyses conclude that there is no association between leisure-time PA and risk of AF [152, 174], and a Norwegian study by Thelle, *et al*, suggest an increased risk of AF in absence of concomitant heart disease (lone AF) by self-reported leisure-time PA at age 40 [145].

While endurance exercise seems to increase the risk of AF, PA might reduce the risk through a preventive effect on AF risk factors like CHD, hypertension and diabetes

mellitus (Figure 3). Therefore, the prevalence of risk factors others than exercise in the studied population will influence the estimated association between exercise and AF. In older populations, where these risk factors are likely to be more prevalent than in younger populations, a stronger AF risk reduction by PA might be expected. This might be important also after adjustment concomitant diseases, as cardiovascular conditions might be unrecognized in many studies.

There is a strong positive association between age and risk of AF [68]. At the same time, older individuals are more likely to report a high number of years of cumulative years of exercise than younger. The prevalence of AF was higher than expected in the youngest and lower than expected in the oldest participants of the Birkebeiner Atrial Fibrillation Study, and the effect estimates increased slightly in the sensitivity analysis performed after exclusion of men aged >75 years. This supports that our results are not an effect of increasing age.

Figure 3. Simplified direct acyclic graph (DAG) illustrating the association between physical activity and endurance exercise and atrial fibrillation.

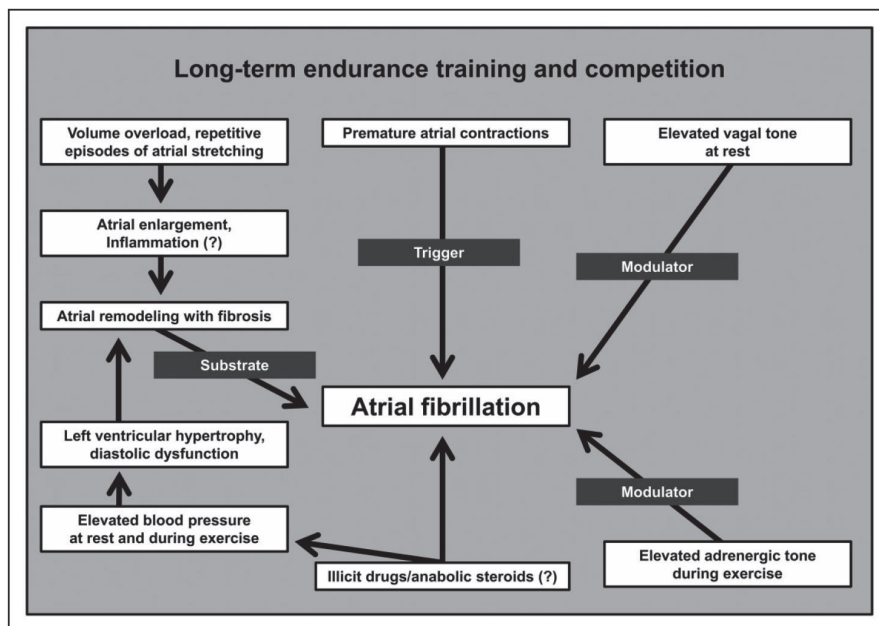


(*) Endurance sport practice is covered by the term physical activity. Due to different underlying mechanisms in the association with AF, self-reported leisure time PA was adjusted for when estimating risk differences for AF.

Arrows and covariates not influencing the analysis are excluded. The highlighted arrow illustrates the direct association between sport practice and atrial fibrillation. The other arrows illustrate intermediate covariates in the association (blue), confounding (red) and colliding (violet) covariates.

Endurance sports like cross-country skiing are highly dynamic sports characterized by a high cardiovascular demand during exercise and competition. During dynamic exercise there is an increase in heart rate, stroke volume, cardiac output and systolic blood pressure [4]. Mechanisms for AF in endurance-trained individuals are not fully understood, but myocardial remodeling and left atrial dilatation related to high volumes and pressures during exercise, atrial fibrosis caused by inflammation, increased vagal tone and electrolyte disturbances during exercise are among the suggested mechanisms [116, 118, 158, 175]. A summary of factors that might influence the development of AF in athletes is shown in figure 4.

Figure 4. Synopsis of factors that might influence the development of atrial fibrillation in athletes, from Wilhelm [158].



Structural myocardial changes like dilatation or fibrosis could cause electrical dissociation between cardiac muscle bundles, and such local electro-anatomical substrates might facilitate re-entry circuits that can induce or maintain arrhythmias [66]. Studies have demonstrated an increase in myocardial biomarkers after endurance sport practice, suggesting an acute effect on the heart, possible caused by volume overload [158, 176]. Other studies have showed that left atrial dilatation is prevalent in many athletes and suggested that this might be a result of chronic exposure to high pressures and volumes [98, 103, 109, 177]. Among veteran Birkebeiner cross-country skiers, left atrial dilatation was identified as a marker for AF [97], but as AF itself might cause atrial dilatation, a causal relationship between atrial remodeling and AF in veteran skiers has not been established. Myocardial edema and inflammation after endurance exercise or competitions have been suggested as underlying mechanisms for myocardial fibrosis in athletes [178, 179].

Finally, the autonomic nervous system seems to play a role. Endurance sport practice is associated with vagal or parasympathetic pre-dominance with low resting heart rates [180]. A high vagal tone might facilitate macro re-entry circuits in the atria by shortening of the atrial refractory period [140, 158], and low heart rates predict AF in men [164]. In a recently published animal study, prolonged endurance exercise was associated with an increased sensitivity to cholinergic stimulation in atrial cardio myocyte potassium channels, that seemed to be mediated through mRNA (messenger Ribonucleic acid) down-regulation of potassium-channel-inhibiting RGS (Regulators of G-protein signaling) proteins [181]. This study supports that enhanced vagal activity plays a central role in the pathophysiology of AF in endurance-trained individuals.

7 CONCLUSIONS

1. Endurance sport practice seemed to be a risk factor for AF in men aged ≥ 65 years.
2. Years of regular endurance exercise were associated with a gradually increased risk of both AF and AFL in men.
3. Prolonged endurance exercise might be associated with an increased risk of AF also in women.
4. AF was associated with poor subjective health, but the vast majority of veteran athletes engaged in regular PA and endurance exercise also after the onset of AF.

8 CONSEQUENCES OF THIS THESIS AND SUGGESTIONS FOR FUTURE RESEARCH

8.1 Consequences of this thesis

This thesis suggests that endurance sport practice and prolonged endurance exercise is associated with an increased risk of AF in men. It demonstrates that AF is prevalent also among female veteran athletes and indicates that prolonged endurance exercise might be associated with the risk of AF also in women.

The literature suggests a complex association between PA, exercise and AF: For the vast majority of the general population, regular PA and exercise probably reduce the risk of AF [112, 119, 143, 144, 173]. On the other hand, this thesis indicates that prolonged and regular endurance exercise might increase the risk of AF gradually on the upper end of the activity range.

It might be reasonable to inform veteran athletes about a possible increased risk of AF, also in the absence of established AF risk factors. At the same time, this thesis has demonstrated that AF do not prevent the majority of veteran athletes from profiting from the benefits of regular PA and exercise. This result supports that, despite a possible increased risk of AF by prolonged endurance exercise, general exercise restrictions should be avoided. Such restrictions could prevent individuals from taking advantage of the health promoting effects of PA and have adverse implications on a public health level [119, 182].

Our current knowledge depends almost exclusively on observational studies, and many questions regarding the duration, intensity and type of exercise that might increase the risk of AF still remain unanswered. Meanwhile, the benefits of regular PA and exercise should be enhanced, and health care workers should recognize their strong responsibility to encourage individuals of all ages to engage in regular PA and exercise [183].

8.2 Suggestions for future research

Future studies of the association between endurance exercise and sport practice and the risk of AF should be prospective with a long follow-up period, include individuals across a broad range of exposure in order to investigate the optimal dose of exercise [132, 182], assess possible confounding factors and include both men and women. Furthermore, future research should focus on determining underlying mechanisms in the association between exercise and AF and include cardiac imaging, biomarkers of inflammation and myocardial fibrosis and electrophysiological studies. Furthermore, they should investigate long-term consequences of AF in veteran athletes. Future studies should include different subtypes of AF, individuals with different stroke risk profiles, record

co-morbid conditions and OAC and investigate the natural course of AF in athletes, incidence of stroke, heart failure, death and other cardiovascular endpoints.

The participation in endurance sports events has increased, also among women. In this thesis we have demonstrated very high attendance rates in two study populations of veteran athletes. Events with shorter distances than marathons and long-distance cross-country ski races are likely to attract more women, but also men that are less exposed to endurance exercise than participants in long-distance endurance events. Therefore, in order to gain a high attendance, a broad range of exposure and a sufficient number of female study participants, the use of participation lists from different endurance sports events might be a feasible method to recruit participants to further studies. Dependent on the study size and resources, health outcomes might be registered by self-reports, ECGs or national health registers, and outcome measurements should be validated, for instance by using handheld recording devices.

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10 PAPERS

Increased risk of atrial fibrillation among elderly Norwegian men with a history of long-term endurance sport practice

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Atrial fibrillation (AF) is the most common cardiac arrhythmia. The prevalence increases with increasing age. In middle-aged men, endurance sport practice is associated with increased risk of AF but there are few studies among elderly people. The aim of this study was to investigate the role of long-term endurance sport practice as a risk factor for AF in elderly men. A cross-sectional study compared 509 men aged 65–90 years who participated in a long-distance cross-country ski race with 1768 men aged 65–87 years from the general population. Long-term endurance sport practice was the main exposure. Self-reported AF and covariates were

assessed by questionnaires. Risk differences (RDs) for AF were estimated by using a linear regression model. After multivariable adjustment, a history of endurance sport practice gave an added risk for AF of 6.0 percent points (pp) (95% confidence interval 0.8–11.1). Light and moderate leisure-time physical activity during the last 12 months reduced the risk with 3.7 and 4.3 pp, respectively, but the RDs were not statistically significant. This study suggests that elderly men with a history of long-term endurance sport practice have an increased risk of AF compared with elderly men in the general population.

Marathons and long-distance cross-country ski races have become increasingly popular, also at higher ages. Young and middle-aged male endurance athletes seem to have an increased risk of atrial fibrillation (AF) (Karjalainen et al., 1998; Elosua et al., 2006; Molina et al., 2008; Graff-Iversen et al., 2012; Müller-Riemenschneider et al., 2012; Andersen et al., 2013) but the role of endurance sport practice as a risk factor for AF among elderly people has only been studied to a small extent.

AF is the most common cardiac arrhythmia, with a prevalence of 1.5–2% in the general population (Camm et al., 2012). The prevalence increases with increasing age, to 10% among 75-year-olds and between 15 and 20% in people aged over 85 years. The prevalence is highest among men, around 15% by 75 years of age (Heeringa et al., 2006; Tveit et al., 2008). The positive association with age is partly explained by increasing prevalence of risk factors for AF. Coronary heart disease (CHD), hypertension and diabetes are among the most

important risk factors (Kirchhof et al., 2012), and are all preventable by regular physical activity (PA).

However, it has been hypothesized that long-term endurance sport practice facilitates structural changes in the heart, increased vagal tone and bradycardia, which could predispose to AF (Calvo et al., 2012; Patil et al., 2012; Turagam et al., 2012; Wilhelm, 2013). Many elderly participants in long-distance endurance sports events have been exposed to endurance sports for many years. Elderly people might be more vulnerable than younger people, due to CHD, hypertension and other factors predisposing to AF, so that the association between endurance sport practice and risk of AF might be even stronger in this population. However, elderly people with a history of long-term endurance sport practice might also have a lower risk of AF, due to the protective effect of PA on important risk factors.

We are aware of only two studies that address the association between leisure-time PA (LTPA) and risk of AF in elderly people; the Cardiovascular Health Study and the Physicians Health Study (Mozaffarian et al., 2008; Aizer et al., 2009). Most participants in these studies were less physically active than required for endurance sport practice and neither of these studies

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demonstrated increased risk of AF associated with PA in elderly people.

CHD among Norwegian long-distance cross-country skiers was studied by Lie and Erikssen in the 1970s. They found a low incidence among the skiers after 5 years follow-up (Lie & Erikssen, 1984). After a 28–30-year follow-up of the same cohort, Grimsmo et al. (2010) demonstrated a high prevalence of AF among the elderly skiers, but the skiers were not compared with a control group.

The aim of our study was to investigate the role of long-term endurance sport practice as a risk factor for AF in elderly men, by comparing the prevalence of AF among participants of a long-distance cross-country ski competition with the prevalence of AF in the general elderly population.

Materials and methods

Design and study populations

The Birkebeiner Ageing Study (BiAS) is a longitudinal study of skiers aged 65 years and older participating in the Norwegian Birkebeiner cross-country ski race, with the main purpose to study associations between long-term exercise and health in advanced age. With a course of 54 km and a total of about 1000 uphill altitude meters, the Birkebeiner race is among the world's most challenging. Based on result lists provided by the organizer, all 658 Norwegian skiers aged 65 years and older who completed the race in 2009 or 2010 were invited to participate. A questionnaire and an invitation letter were sent to the participants, and the completed questionnaire was returned by post. Due to low number of female participants in BiAS, only men were included in this study.

In order to assess the association between endurance sport practice and risk of AF, cross-sectional baseline data from BiAS were compared with data from the sixth survey of the Tromsø Study (Tromsø 6) which took place in 2007–2008. The Tromsø Study is a population-based general health study with repeated cross-sectional surveys in the largest city in Northern Norway (Jacobsen et al., 2012). In Tromsø 6, 19 762 inhabitants in Tromsø aged 30 years and older were invited. A total of 12 982 participated (66%).

For this study, 1768 out of 2757 invited men aged 65 to 87 years were included from Tromsø 6 (67.7%). From BiAS, 509 out of 607 invited men aged 65 to 90 years were included (83.9%).

The Tromsø Study was approved by the Norwegian Data Inspectorate and the Norwegian Directorate of Health. Both studies were approved by the Regional Committees for Medical and Health Research Ethics, and comply with the Declaration of Helsinki. All participants gave informed written consent.

Assessment of atrial fibrillation, physical activity and exercise

AF was assessed with the question "Do you have, or have you had atrial fibrillation?" in both studies.

In both studies, an identical question with a four-level scale was used to assess LTPA: "How physically active have you been during the past year in your leisure time. If your activity level varies between summer and winter, note an average value. Tick one only." Levels of activity were defined as follows: (a) sedentary (reading, watching television, other sedentary activity); (b) light PA (walking, cycling or other activity for at least 4 h per week); (c) moderate PA (light sports, heavy gardening, for at least 4 h per week); (d) high PA (regular hard exercise or competitive sports several times per week). This scale was originally developed by Saltin & Grimby (1968) and was used in middle-aged and elderly Swedish athletes. It discriminates between sedentary persons and

their more active counterparts with respect to maximal oxygen uptake (Saltin, 1977), and has been validated in the Tromsø population (Emaus et al., 2010).

The participants in BiAS were asked for the total number of years they had practiced systematic endurance training, the age when they first participated in the Birkebeiner race, how many years they had participated in the race, and how many Birkebeiner medals they had won. Participants with a finishing time not exceeding 25% of the average finishing time of the five fastest participants in each 5-year age class are awarded a Birkebeiner medal.

Assessment of health status and other characteristics

Age was registered at inclusion. Body mass index (BMI) was calculated as weight (kg) divided by squared height (m). CHD was assessed with the two questions "Have you had a heart attack?" and "Do you have or have you had angina pectoris?" Hypertension was assessed with the question "Do you take or have you ever taken blood pressure lowering medicines?" Diabetes was assessed with the question "Do you have diabetes?" Education level, health status, smoking habits and alcohol consumption were assessed with slightly different questions and categories, and recoded into common categories. In Tromsø 6, height and weight were measured with subjects wearing light clothing and no shoes. Except from height and weight in Tromsø 6, all variables were self-reported by questionnaires, with only minor differences between the studies. English translations are available on websites (<http://www.kavlisenter.no>; <http://www.tromsostudy.com>).

Statistical analysis

Characteristics of the study populations were compared by Student's *t*-test for means of continuous variables and Pearson's Chi-square of independence for categorical variables.

A history of endurance sport practice, defined as belonging to the study population of skiers, was the main exposure. Total prevalence and prevalence after exclusion of persons with CHD were reported for the variable self-reported AF outcome.

Both study populations were analyzed together in a linear regression model with a robust variance estimator. The model gives risk differences (RDs) with 95% confidence intervals (CI) for AF. When designing the model, a direct acyclic graph (DAG) was used to identify covariates that are appropriate for adjustment. The DAG shown in Figure 1 is simplified to aid readability. Covariates and arrows not influencing the analysis are excluded. The highlighted arrow represents the direct association between endurance sport practice and AF. CHD, hypertension, diabetes, age, height, BMI, education level, alcohol consumption, smoking habits and LTPA were adjusted for in the model. Health consciousness in the DAG represents unmeasured confounding lifestyle factors. In the variable "number of alcohol units usually consumed when drinking," there were over 10% missing data among the skiers. Analysis after exclusion of cases with missing data for alcohol consumption did not change the effect estimates.

Since odds ratios (ORs) are commonly reported for binary outcomes like AF, we also report results from a logistic regression model using the same covariates as the linear model.

All statistical analyses were conducted using SPSS version 20.0 (IBM, Armonk, New York, USA).

Results

Some characteristics of the study populations are shown in Table 1. Participants in BiAS were on average 2.7 years younger, had a lower BMI, and were taller compared with the general population. Higher proportions of the skiers reported college or university education and

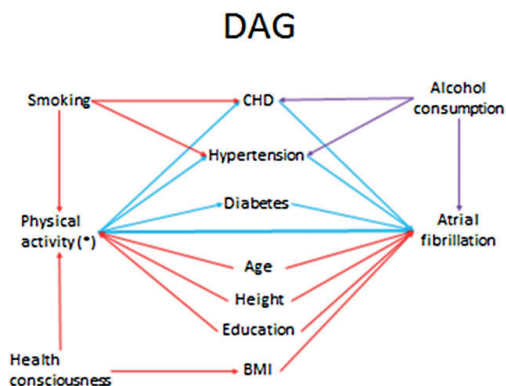


Fig. 1. Simplified direct acyclic graph (DAG). Arrows and covariates not influencing the analysis are excluded. The highlighted arrow illustrates the direct association between sport practice and atrial fibrillation. The other arrows illustrate intermediate covariates in the association (blue), confounding (red) and colliding (violet) covariates.

(*) Endurance sport practice is covered by the term physical activity. Due to different underlying mechanisms in the association with AF, self-reported leisure time PA was adjusted for when estimating risk differences for AF.

current full-time employment. There were fewer smokers and more alcohol consumers among the skiers. They also reported higher levels of LTPA and valued their own health as better than the general population in Tromsø. All these differences were statistically significant. Among the skiers, the average BMI was normal and the prevalence of traditional risk factors for AF was very low. The crude prevalence of AF was 13.2% in the skiers and 11.6% in the general population. The prevalence of AF after exclusion of persons with CHD was 13.0% in the skiers and 9.8% in the general population.

Figure 2 and Supporting Information Table S1 show adjusted RDs with 95% CIs by selected covariates based on the linear regression model. The constant term shown in the first line of the table describes the risk of AF for a reference person, and was estimated to 11.3%. This equals the expected prevalence of AF when all covariates are set at their reference values. Endurance sport practice gave an added risk for AF of 6.0 percent points (pp) (95% CI 0.8–11.1). The risk of AF increased with 0.4 pp per added year of age. The risk of AF increased with 0.3 and 0.6 pp per cm of height and unit of BMI added, respectively. Also hypertension and CHD were associated with added risk for AF. RDs were not significant for diabetes, smoking, lipid-lowering treatment or alcohol consumption (Fig. 2).

Example

The estimated risk of AF for a sedentary 71-year-old man, 175 cm tall, with a BMI of 26.3, non-smoker with average alcohol consumption and education level, no CHD, diabetes

or hypertension and not practicing endurance sports was 11.3%. For a man with the same characteristics but who practices endurance sports, the estimated risk was 13.0% if reporting moderate PA (11.3+6.0–4.3%), and 17.6% if reporting the highest level of PA (11.3+6.0+0.3%).

Associations expressed as relative effects (ORs) were calculated by logistic regression. The adjusted OR (aOR) for AF in men practicing sport was 1.28 (95% CI 0.94–1.73) after adjustment for age and 1.90 (95% CI 1.14–3.18) after multivariable adjustment for age, traditional risk factors for AF and education. After exclusion of persons with CHD and multivariable adjustment, the aOR for AF was 1.81 (95% CI 1.04–3.14) ($n = 1713$).

Sensitivity analysis after exclusion of skiers who had participated less than three times in the Birkebeiner race did not change the effect estimates.

Discussion

This study suggests that elderly men with a history of long-term endurance sport practice have a higher risk of AF than elderly men in the general population. Light and moderate LTPA during the previous year may reduce the risk of AF, although this is not statistically significant in this study.

Our study confirms earlier findings of a high prevalence of AF among elderly male long-distance cross-country skiers (Grimsmo et al., 2010), and the association between repeated participation in long-distance cross-country ski races and increased risk of AF, recently discovered among Swedish skiers (Andersen et al., 2013). Consistent with previous results from Tromsø (Nyrmes et al., 2013), we did not find an increased risk of AF associated to level of LTPA. In contrast, recently published results from a large population-based study indicate that LTPA is associated with an increased risk of AF in the middle-aged general population (Thelle et al., 2013). The cohorts in these two studies were younger than our study populations.

In accordance with previous studies, both body height and BMI were positively associated with the risk of AF (Mont et al., 2008; Nyrmes et al., 2013). The added risk of AF per unit of BMI of 0.7 pp is similar to the OR of 1.08 for AF per unit of BMI found in a population-based cohort of Danish men (Frost et al., 2005).

Study population

In the Cardiovascular Health Study of elderly people, the most active people had the lowest incidence of AF [hazard ratio (HR) 0.64, 95% CI 0.52–0.79] (Mozaffarian et al., 2008) but they reported exercise corresponding to an average of only 1840 kilocalories per week, which is probably much less than average in our study population. Interestingly, exercise intensity was associated with risk of AF in a U-shaped pattern: While moderate intensity was associated with lower incidence

Table 1. Characteristics of participants of the Birkebeiner cross-country ski race and the general population in Tromsø, men 65–90 years old

	Athletes <i>n</i> = 509 Mean (median, range)	General population <i>n</i> = 1867* Mean
Age	68.9	71.6
Height	178.5	174.3
Body mass index	23.6	27.0
Age at first Birkebeiner race participation	43.6 (42, 18–76)	–
Number of completed Birkebeiner races	17.0 (14, 1–53)	–
Number of achieved Birkebeiner medals	11.5 (6, 0–49)	–
Total years of systematic endurance training	33.2 (34, 1–67)	–
	% of 509	% of 1867
Live with a spouse or partner	88.2	79.1
College or university education	41.0	28.5
Occupation		
Retired	60.9	86.1
Full-time work	37.9	9.1
Good or excellent self-reported health status	86.2	60.3
Self-reported leisure-time physical activity		
Sedentary	0.2	19.4
Light	9.9	58.0
Moderate	50.9	21.9
High	39.0	0.7
Frequency of alcohol consumption		
Never	9.6	14.2
1–4 times a month	72.6	64.0
2–3 times a week	14.7	15.6
4 or more times a week	3.1	6.2
Daily smoking		
Current daily smoker	0.8	15.4
Previous daily smoker	28.5	60.6
Never smoked daily	70.7	24.0
Coronary heart disease	3.1	23.8
Diabetes	0.8	8.2
Current or previous lipid-lowering treatment	14.3	33.0
Current or previous antihypertensive treatment	14.9	39.0

*All *P*-values ≤ 0.001 .

of AF, people reporting the highest intensity had the same incidence as people not exercising. In The Physicians Health Study, no association was found between exercise frequency and risk of AF in physicians aged 50–84 years, although the most active doctors exercised five to seven days per week (Aizer et al., 2009).

In our study, 61% of the skiers reported LTPA below the highest level during the last 12 months. This might be important in the interpretation of our results, as the increased risk of AF associated with endurance sport practice might partly be balanced by light or moderate PA. This reduction in AF risk might be explained by a reduced prevalence of AF risk factors, as demonstrated in the DAG (Fig. 1).

The added risk of AF by long-term endurance sport practice found in our study corresponds to an aOR of 1.90 (95% CI 1.14–3.18). A meta-analysis reported an OR for AF of 5.3 (95% CI 3.6–7.9) in athletes compared with non-athletes (Abdulla & Nielsen, 2009). The higher ORs reported in the meta-analysis and previous publications (Karjalainen et al., 1998; Elosua et al., 2006; Molina et al., 2008) might reflect exposure to sport practice at higher levels than in our non-elite skiers, that different

types of endurance sports might be differently associated to the risk of AF, or that the volume of training between competitions varies between the study cohorts.

Control group

Even more importantly, the prevalence of AF in the control groups influences the effect estimates strongly. While the Finnish orienteering runners in Karjalainen et al.'s study (1998) were compared with middle-aged men with a low prevalence of AF, the skiers in our study were compared with the general population with an AF prevalence of 11.6%. The comparison of a highly selected cohort of skiers with the general population might be questioned. However, a control group of elderly people with very low prevalence of traditional risk factors for AF and without a history of endurance sport practice might be difficult to find. In the study of Swedish long-distance cross-country skiers, the HR for AF among participants who had completed five or more races was only 1.29 (95% CI 1.04–1.61), and no significant association was found between finishing time and AF risk. The lack of comparison of the skiers with inac-

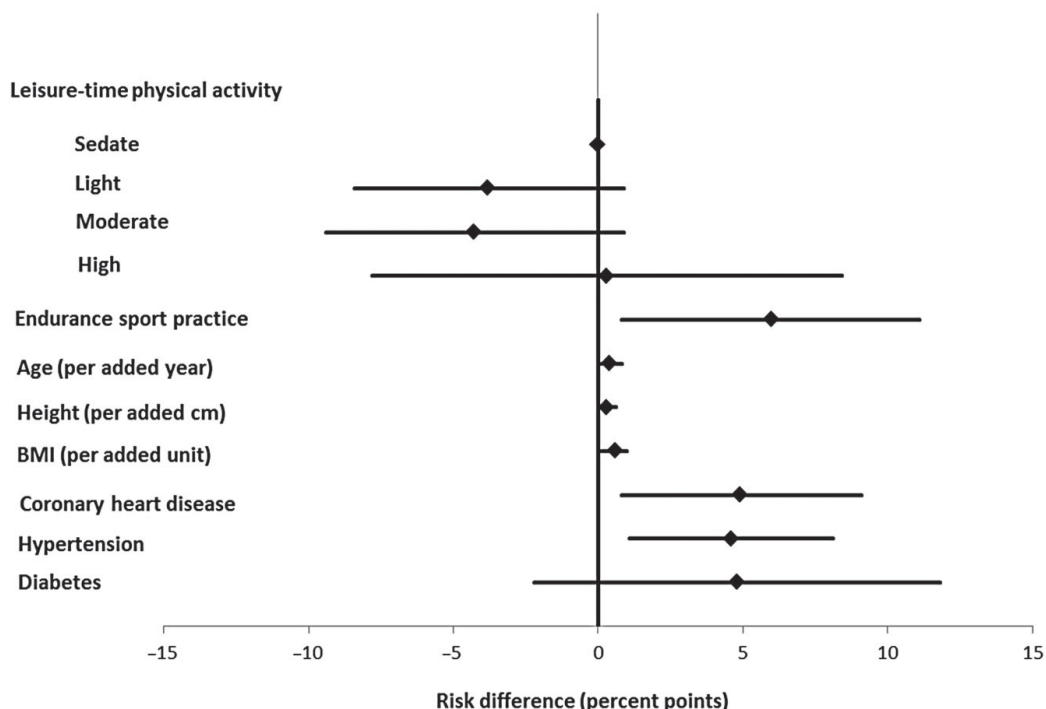


Fig. 2. Studied risk factors for atrial fibrillation. Estimated atrial fibrillation risk differences with 95% confidence intervals by selected covariates. Both study populations analyzed together, men 65–90 years old.

tive people is discussed by the authors as an important limitation of the study (Andersen et al., 2013).

Age

Age is another factor with an impact on effect estimates and the younger age of the cohort of Swedish skiers probably contributes to the weaker association. Long-term PA and endurance sport practice reduces the risk of CHD, hypertension and diabetes. These are all important risk factors for AF and are increasingly prevalent with increasing age. While the relative importance of other modifiable risk factors decreases with increasing age, PA is shown to be a robust health-promoting factor in elderly people (Gulsvik et al., 2011). It is unclear how a potentially stronger beneficial effect of exercise in this age group might influence the risk of AF. In the heterogeneous group of elderly, there might be both individuals who benefit from their history of endurance sport practice with reduced risk of AF and individuals who experience an increased risk due to age-related vulnerability to strenuous endurance sport practice.

Strengths

The main strength of the study is the unique sample of elderly and active long-distance cross-country skiers,

which on average has been exposed to endurance sport practice over many years at a much higher level than the general population. Previous studies of the association between sport practice and risk of AF have been questioned (Delise et al., 2012) because many of the participants were exposed to cardiovascular risk factors like smoking (Molina et al., 2008). The low prevalence of traditional risk factors for AF in BiAS is another asset of our study. Very few of the skiers were smokers, had CHD or diabetes, and the prevalence of hypertension was much lower than in the general population. Due to the high response rate of almost 84%, we assume the study population in BiAS to be representative for elderly men participating in long-distance endurance competitions. Finally, our results are strengthened by multivariable adjustment for possible confounding from various life style factors, health conditions and socioeconomic status.

Limitations

The main limitation of the study is self-reporting of AF. AF often remains unrecognized for a long time, especially in elderly people (Engdahl et al., 2013) and because AF is often paroxysmal, the diagnosis might be difficult to confirm. Palpitations and other symptoms

might be interpreted as AF, leading to false positive reports. Thus, the validity and completeness of the outcome measure is a weakness of many studies assessing prevalence or risk of AF. The skiers might also be more aware of heart rhythm disturbances than others and more interested in participating in the study, which could possibly lead to an overestimation of the risk of AF in this population.

The cross-sectional design limits the possibility to investigate causal associations, as it is unclear if the outcome has preceded the exposure. However, in this study it is unlikely that AF has preceded the participation in endurance sport, as most participants have practiced long-distance cross-country skiing for many years.

Endurance sport practice was not recorded in Tromsø 6. We assume from the low number of participants reporting the highest levels of LTPA that the number of subjects participating in long-distance endurance competitions in this study population is low or zero and that the difference between the study populations could therefore be interpreted as binary. However, this could lead to an underestimation of the effect estimate in our study.

Elderly populations are heterogeneous and, despite adjustment for chronological age, the degree of biological ageing is likely to be differential between the study populations, as expressed by differences in CHD and cardiovascular risk factors. The study populations may also differ in terms of unmeasured characteristics. In population-based studies, the proportions of people with ethnic minority background (Christensen et al., 2012) and with poor health status (Knudsen et al., 2010) tend to be larger among non-responders than among responders and this trend tends to counteract selection bias in our study. However, selection bias may have influenced our results.

People without AF are more likely to continue participation in long-distance endurance sport competitions into old age, corresponding to a healthy worker effect (Thygesen et al., 2011). This assumption is supported by the fact that there were no cases of AF among the skiers

aged 80 years and older and probably leads to an underestimated risk of AF among the skiers. On the contrary, some skiers with AF might have been motivated to continue skiing because of the beneficial effects of exercise.

Perspective

This study adds to the current knowledge regarding the association between endurance sport practice and risk of AF. In elderly men, a history of endurance sport practice was found to be a risk factor for AF with an effect comparable to traditional risk factors for AF like CHD and hypertension. Light or moderate LTPA during the last 12 months seems to partly balance the increased risk of AF. It is still unclear if sport practice in different life phases influences the risk of AF differentially and how AF in this population of very active elderly men might influence the risk of stroke. Regular PA reduces mortality, functional decline and the risk of several age-related diseases. Elderly people should therefore be encouraged to be physically active.

Key words: sports cardiology, arrhythmias, endurance exercise, master athletes, elderly, cross-country skiing, skiers, heart disease.

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Supporting information

Additional Supporting Information may be found in the online version of this article at the publisher’s web-site:

Table S1. Estimated atrial fibrillation risk differences for endurance sport practice and other selected covariates. Both study populations analyzed together, men 65–90 years old.

Table S1 (supporting information): Estimated atrial fibrillation risk differences for endurance sport practice and other selected covariates. Both study populations analyzed together, men 65-90 years old.

	Risk difference %	95 % Confidence intervals
Constant term (*)	11.3	
Level of self-reported leisure-time PA		
Sedate	0 (ref)	
Light	- 3.7	(-8.4 – 0.9)
Moderate	- 4.3	(-9.4 – 0.9)
High	+ 0.3	(-7.8 – 8.4)
Endurance sport practice	+6.0	(0.8 – 11.1)
Age (per added year)	+0.4	(0.1 – 0.8)
Height (per added cm)	+0.3	(0.1 – 0.6)
BMI (per added unit)	+0.6	(0.1 – 1.0)
CHD	+ 4.9	(0.8 – 9.1)
Hypertension	+ 4.6	(1.1 – 8.1)
Diabetes	+4.8	(-2.2 – 11.8)

(*) The constant term reported is the expected risk of AF for a 71-year old man, 175 cm tall and with a BMI of 26.3, when sedate, not smoking, with an average alcohol consumption and level of education, no CHD, diabetes or hypertension and not practicing endurance sport.

Physical activity, symptoms, medication and subjective health among veteran endurance athletes with atrial fibrillation

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Key words: Atrial fibrillation, endurance exercise, veteran athletes, physical activity, sports cardiology

Abstract

Background Atrial fibrillation (AF) is highly prevalent but has not previously been characterized in detail in veteran athletes. We aimed to describe physical activity (PA), symptoms, medication and subjective health in relation to AF subtype and co-morbidity among veteran cross-country skiers with AF.

Methods In total, 4952 Norwegian men and women aged 53-85 years took part in this cohort study, 2626 veteran cross-country skiers and 2326 from the general population. PA, endurance exercise, functional capacity, co-morbidity, drug use and subjective health were self-reported by questionnaires. AF was self-reported and confirmed by electrocardiograms in a medical record review.

Results The prevalence of self-reported AF among veteran skiers was 12.3%. AF was confirmed in 140 skiers and 118 individuals from the general population. Among skiers with AF (mean age 69 years), 52% had paroxysmal, 23% persistent and 24% permanent AF. AF was associated with poor subjective health, but 89% of the veteran skiers were physically active and 64% engaged in regular endurance exercise after the onset of AF. While 59% had experienced palpitations during the past year, 32% reported reduced functional capacity. Two out of three with AF and a CHA₂DS₂-VASc score ≥ 2 used oral anticoagulants (OAC).

Conclusions AF was associated with poor subjective health, but the vast majority of veteran athletes engaged in regular PA and endurance exercise also after the onset of AF. This is important, as PA and exercise might reduce AF symptoms, mortality and morbidity. Many veteran skiers with AF were not optimally treated with OAC.

Abstract word count: 248

Introduction and background

Atrial fibrillation (AF) is the most common clinically significant cardiac arrhythmia, and the prevalence is strongly related to age [1]. While uncommon at younger ages, the prevalence rises from 1-4% at age 60 to >15% in populations aged >80 years [2,3]. In the short term, AF is associated with symptoms, reduced physical capacity, drug use and poor subjective health [4,5]. In the long term, AF is associated with an increased risk of stroke and risk assessment using the CHA₂DS₂-VASc score has been recommended [1]. Individuals with AF and a CHA₂DS₂-VASc score ≥ 2 should be treated with oral anticoagulants (OACs), but the adherence to such treatment is unsatisfactory [6,7].

While moderate physical activity (PA) reduces the risk of both AF and other cardiovascular diseases in older adults [8,9], AF is highly prevalent among veteran endurance athletes [10,11]. The number of individuals aged >40 years that engage in endurance sports events is increasing [12,13], but AF has not previously been characterized in detail in veteran athletes. In individuals with AF, regular exercise might reduce symptoms and improve functional capacity [14]. Thus, engagement in PA after onset of AF is crucial, both in the short term and in order to profit from the universal long-term benefits of regular exercise [15]. We are not aware of any studies that have addressed PA and exercise among veteran athletes with AF.

AF symptoms might be due to the arrhythmia or due to co-morbidity and symptoms vary between different AF subtypes. Few studies have differentiated between paroxysmal, persistent and permanent AF or between AF with and without co-morbid conditions [5].

We aimed to describe PA, functional capacity, palpitations, medication and subjective health related to AF subtypes and co-morbidity among Norwegian veteran cross-country skiers, and to compare veteran athletes and individuals from the general population with AF.

Methods

Study populations

All 3,485 individuals who were aged ≥ 40 years and participated in the Birkebeiner cross-country ski race in 1999, and had a Norwegian postal address, were invited to participate in this cohort study.

Cross-country skiing has been classified as a highly dynamic sport with moderate to high cardiovascular demand during competition [16], and the 54-kilometre Birkebeiner race is among the world's most challenging cross-country ski-races.

Meanwhile, 4,015 men and women who had previously taken part in the population-based Oslo Health Study in 2000-01 and 2009 and were aged ≥ 50 years in 2009 were also invited to participate. A flow chart describing the inclusion process is shown in the supplementary figure 1.

During 2012, both the veteran skiers and the participants from the Oslo Health Study received an identical postal questionnaire (supplementary data) together with an invitation letter.

The study was approved by the Regional Committee for Medical and Health Research Ethics and complies with the Declaration of Helsinki. Approvals for the review of the medical records were obtained from the responsible authorities for research and data protection for each hospital.

Atrial fibrillation and co-morbid conditions

Self-reported AF was defined by positive response to at least one of the two questions "Do you believe that you have or have had atrial fibrillation?" or "Have you been diagnosed as suffering from atrial fibrillation by a doctor?" in the questionnaire. Co-morbid conditions (myocardial infarct, angina pectoris, coronary bypass, cardiac valve replacement, stroke, diabetes mellitus, hyperthyroidism) were assessed with the question "Do you have or have you ever had (name of disease)?" Concomitant heart diseases were condensed into one variable. CHA₂DS₂-VASc score was estimated using age, sex and self-reported coronary heart disease, hypertension, stroke and diabetes mellitus.

During 2013 medical records were reviewed in subjects who reported AF, gave consent and named a Norwegian public hospital where they were diagnosed. Incident arrhythmias up until

31.12.2012 were identified by electrocardiograms (ECGs). Atrial flutter was not assessed in the questionnaire, and because of the close interrelationship between AF and atrial flutter, both arrhythmias were classified together as AF. The following subtypes of AF were self-reported and supplemented with data from the medical records: Paroxysmal (attacks that end by themselves or with medical treatment), persistent AF (attacks that are only alleviated by intravenous treatment or electric shock) and permanent (AF the entire time). Paroxysmal and persistent were classified together as non-permanent AF. If the review did not reveal other relevant concomitant conditions (heart disease, diabetes, hyperthyroidism, acute infection, surgery during the past seven days), the arrhythmia was classified as AF without co-morbidity. In individuals with hypertension the arrhythmia was classified as without co-morbidity if echocardiography findings were available and normal.

Physical activity and exercise

Leisure-time PA during the past year was assessed with the question “State the movement and PA you engage in during your leisure time. If your activity level varies between summer and winter, note an average value. Tick the most appropriate box only”. A five-level scale was condensed into the four categories: 1) Sedentary (reading, watching television, other sedentary activity); 2) Light PA (walking, cycling or other activity for at least 2 hours per week); 3) Moderate PA (light sports, heavy gardening, for at least 4 hours per week); and 4) High PA (Regular hard exercise or competitive sports several times per week). This scale was originally used among middle-aged and elderly Swedish athletes in the 1960's [17], and is validated among Norwegian men [18,19]. The participants were asked if they still engaged in regular endurance exercise, defined in the questionnaire as exercise bouts of ≥ 30 minutes \geq three times per week with the goal of improving endurance capacity. They were also asked to report if they were still participating in the Birkebeiner race, and to give the reason for no longer participating in the race.

Functional capacity, palpitations, medication and subjective health

Functional capacity was assessed with the New York Heart Association (NYHA) functional classification (class I-IV) [20]. The participants were asked to report how their heart disease impact on

their functional capacity with four answer categories; I) No limitations. Ordinary PA does not cause undue fatigue, dyspnea or chest pain; II) Slight limitations of PA, but comfortable at rest. Ordinary PA results in fatigue, dyspnea or chest pain; III) Marked limitations of PA, but comfortable at rest. Even light PA causes fatigue, dyspnea or chest pain; and IV) Inability to carry on any PA without discomfort. Fatigue or chest pain may be present even at rest. The NYHA classification was originally developed for use in heart failure patients, but has also been used in AF patients in different settings and is a valid measure of functional capacity [5]. The NYHA-classes were condensed into the two categories “no functional limitations” (class I) and “functional limitations” (class II-IV).

Palpitations were assessed with the question “Have you noticed sudden changes in your heart rate or heart rhythm in the past year?” This question was used in the Tromsø Study, a population-based health study in the largest city of northern Norway [21]. Other AF symptoms were not assessed.

The participants reported use of the following medicines: Beta-blockers, calcium-channel-blockers, amiodarone, dronedarone, flecainide, digitoxin, digoxin, acetylsalicylic acid (ASA), warfarin and dabigatran.

Subjective health was assessed with the question “How do you rate your own health?” and the four answer categories were condensed into poor (response to poor or fair) and good (response to good or excellent) health. The question has been used previously in AF patients [4], is a reliable and valid measure of subjective overall health status, including biological, psychological and social dimensions of health, and is associated with morbidity and mortality [22,23].

Statistical analysis

All study participants aged ≤ 85 years were included in this analysis. We used Student’s t-test for means of continuous variables and Pearson’s Chi square of independence for categorical variables to compare characteristics of the study participants. Individuals with missing data in the variable functional capacity (24%) were categorized into NYHA class I. Multivariable logistic regression analysis was used to calculate adjusted odds ratios (aORs) with 95% confidence intervals (CI) for poor subjective health. Adjustments were made for age, sex, body mass index (BMI), concomitant heart

disease, diabetes mellitus, stroke and number of completed Birkebeiner races. All statistical analyses were conducted using SPSS version 20.0 (IBM, Armonk, New York, USA).

Results

After exclusion of 27 individuals aged >85 years, 2626 veteran cross-country skiers (76% of the invited) were eligible for the analyses. AF was reported by 322 (12.3%), medical records were available for review for 177 and AF was confirmed in 140 skiers. Among 2326 participants from the general population, there were 260 cases of self-reported AF of whom 118 were confirmed and included in this analysis. Among veteran skiers, 52% had paroxysmal, 23% had persistent and 24% had permanent AF, while the corresponding proportions in the general population were 52%, 17% and 30%.

Table 1 shows the characteristics of veteran skiers without AF, with confirmed AF, with self-reported but not confirmed AF and individuals with AF from the general population. Skiers with confirmed AF were older and had a higher prevalence comorbid conditions than skiers without AF. The prevalence of stroke was more than twice as high in skiers with AF compared to skiers without AF. Skiers with AF were slightly younger, had lower BMI and less co-morbidity than their counterparts from the general population. There were only two women with AF among the skiers.

Only 11% of the veteran skiers with AF were inactive, 70% reported moderate or high PA during the past year and 64% still engaged in regular endurance exercise at least three times per week. However, a third of the veteran skiers with AF had discontinued their participation in the Birkebeiner race due to the arrhythmia and AF was associated with poor subjective health after adjustment for age, sex, BMI, co-morbid conditions and number of completed Birkebeiner races (aOR of 2.8 (CI 1.7-4.6)). The corresponding estimate for AF without co-morbidity was 1.9 (CI 0.9-3.9).

Palpitations during the past year were reported by 59% of the veteran skiers and 68% in the general AF population. Reduced functional capacity (NYHA II-IV) was prevalent in 32% and 33%, respectively. Poor subjective health was less common in skiers with AF compared to individuals with

AF in the general population (18% versus 31%), but did not differ after multivariable adjustment (data not shown). Veteran skiers were more active and used less rate-controlling drugs (43% vs. 73%). Table 2 shows PA, functional capacity, palpitations, AF medication and subjective health according to subtype of AF in skiers and the general population. Skiers with permanent AF were less active than skiers with non-permanent AF, while there was no difference in PA between the AF subtypes in the general population. Palpitations, functional capacity, medication and subjective health did not differ significantly between the AF subtypes.

Out of 62 veteran skiers with AF and an estimated CHA₂DS₂-VASc score ≥ 2 , 41 (66%) used OAC, 9 (15%) used ASA and 12 (19%) were untreated. In the general AF population, 54 out of 86 with an estimated CHA₂DS₂-VASc score ≥ 2 (63%) used OAC and 16 (19%) used ASA. The proportion treated with OAC was highest in permanent AF (87%) and lowest in paroxysmal AF (51%).

In the review of medical records, 57% of the veteran skiers and 42% in the general population were classified as AF without co-morbid conditions. Table 3 shows characteristics according to co-morbidity. Individuals with AF without co-morbid conditions were more physically active and reported better subjective health than those with co-morbidity. Palpitations, functional capacity and use of rate-controlling drugs did not differ between the two groups.

Characteristics and triggers of AF attacks in veteran skiers and the general population with non-permanent AF (n=184) are shown in the supplementary table 1. Palpitations during the past year and frequency of AF attacks did not differ between the two groups. Among the veteran skiers, paroxysms were triggered by exercise in 25% and often occurred in relation to typical vagal triggers.

Discussion

In this study we have described AF in detail in veteran athletes and demonstrated that the vast majority engaged in regular PA and endurance exercise even after the onset of AF.

AF was highly prevalent among the veteran athletes in this study [24]. This is in line with results from previous studies of Norwegian cross-country skiers [10,11], and supports that endurance sport practice might be associated with an increased risk of AF [25,26].

More than 50% of the skiers with AF experienced palpitations during the past year and one out of three reported reduced functional capacity. Palpitations have been reported to occur more frequently in athletes with AF than in general AF populations [27], but did not differ between the AF subpopulations in our study. In both groups, symptoms were less frequent than in previous studies [28,29]. This might be explained by differences in the distribution of AF subtypes and co-morbidity between studies. In this study, palpitations and functional capacity reduction did not differ between the AF groups with and without co-morbid conditions. On the other hand, poor subjective health was more common in individuals with co-morbidity. A previous study suggested that AF is well tolerated in athletes [30], and our result might support that subjective health depends on comorbid conditions among veteran athletes with AF.

Two out of three with an estimated CHA₂DS₂-VASc score ≥ 2 used OAC. Although self-reports might provide imprecise information on adherence to OAC treatment and the stroke risk score is roughly estimated in this study [31], this result indicates that one out of three is not optimally treated. Only 3% used dabigatran, while the remaining 97% used warfarin. Dabigatran was introduced first and was the only among the novel oral anticoagulants (NOACs) that was investigated in this study. None of the NOACs were used routinely in Norway at the time of this study [32].

The proportion using rate-controlling drugs was lower among the skiers compared to the general AF population in our study, but higher than in the ALFA study conducted in France during the 1990's [33]. This might reflect differences in AF medication prescription between countries and over time. Our clinical experience is that endurance-trained individuals often have lower heart rates without medication, and that active individuals often refuse to use beta-blockers due to side effects.

In the general population, stress was the most commonly reported trigger for AF attacks. This is in line with results from a previous study among 100 Swedish AF patients seeking hospital

assistance [34]. Vagal triggers were more common in veteran skiers, reflecting different underlying mechanisms of AF [26,35,36].

Limitations

Because AF might be asymptomatic and is impossible to detect between attacks in individuals with paroxysmal AF, the prevalence of AF might be underestimated in our study. On the other hand, AF is often asymptomatic [1], and because AF was confirmed in hospital, symptoms are likely to be overestimated among the athletes with confirmed AF. The validity and reliability of self-reporting of AF symptoms and subjective health are unknown, but in general, athletes might be more prone to report symptoms than others. Other symptoms than palpitations were not assessed and established scoring systems for AF symptoms were not used in this study [5]. Cardioversion and ablation might influence both symptoms, PA and the use rate-controlling drugs and OAC [37], but these treatments were not investigated in this study. The direct comparison between the two AF subpopulations in the study is hampered by the low number of women with AF and lower proportion with permanent AF among the skiers. The underlying mechanisms for AF are likely to differ between the subpopulations [26], as indicated by a higher proportion with AF in absence of co-morbid conditions and typical vagal triggers for AF paroxysms among the skiers.

Strengths

The population of veteran athletes exposed to prolonged endurance exercise is a main strength of this study. This, in addition to the validation of AF diagnoses by review of medical records, the differentiation between AF subtypes and the collection of data on co-morbid conditions, enabled a detailed characterization of AF in a growing subpopulation, namely older individuals exposed to prolonged endurance exercise with low co-morbidity but increased risk of AF. Although the study population of veteran athletes is selected, the high response rate of 76 % is another asset of this study and we believe that our results might be generalizable to other populations of veteran athletes who have been performing at a high competitive level with prolonged endurance exercise [36].

The design of this study does not allow conclusions regarding beneficial effects of exercise, and further studies should address whether veteran athletes with AF might also benefit from regular exercise in terms of reduced symptom burden, improved exercise capacity, decreased heart rate, improved heart rate variability and increased quality of life [38,39]. It remains unclear whether the stroke risk in veteran athletes with AF is comparable to that of general AF populations. Until the long-term consequences of AF in this part of the population has been investigated in prospective studies, veteran athletes with AF should be treated in line with current guidelines [1].

Conclusions

AF was associated with poor subjective health among veteran athletes with AF, but the vast majority of veteran athletes still engaged in regular PA and endurance exercise after onset of AF. This is important, as PA and exercise might reduce AF symptoms, and in the long term probably reduce mortality and morbidity. Many veteran athletes with AF were not optimally treated with OAC in order to prevent stroke.

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Conflict of interests

Marius Myrstad has received a personal honorarium for a lecture from MSD. The other authors have nothing to disclose.

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Table 1: Characteristics of the study populations. Men and women aged 53-85, n=2747.

	Veteran skiers without AF n=2304	Veteran skiers with confirmed AF n=140	Veteran skiers with self-reported AF n=185	General population with AF n=118
	<i>Mean (median, range)</i>	<i>Mean (median, range)</i>	<i>Mean (median, range)</i>	<i>Mean (median, range)</i>
Age (years)	64.0 (63, 53-85)	68.5 (69, 53-85)	64.9 (65, 53-85)	69.8 (71, 56-73)
Body mass index (kg/m²)	24.1 (23.9, 14.4-40.0)	24.4 (24.2, 19.9-32.4)	24.5 (24.0, 19.4-35.2)	26.2 (25.8, 18.8-43.2)
Education (years)	14.1 (15, 0-30)	13.9 (15, 0-24)	14.2 (15, 0-26)	14.6 (15, 0-31)
Completed Birkebeiner races	13.8 (12, 1-57)	17.3 (15, 1-49)	14.3 (13, 1-45)	-
	<i>n (% of 2304)</i>	<i>n (% of 140)</i>	<i>n (% of 185)</i>	<i>n (% of 118)</i>
Females	274 (12%)	2 (1%)	7 (4%)	35 (30%)
Stroke	89 (4%)	14 (10%)	8 (4%)	14 (12%)
Concomitant heart disease	153 (7%)	24 (19%)	16 (9%)	32 (27%)
Antihypertensive treatment^a	498 (22%)	61 (44%)	51 (28%)	71 (60%)
Diabetes mellitus	86 (4%)	7 (5%)	6 (3%)	14 (12%)
Lipid-lowering treatment*	573 (25%)	51 (36%)	55 (30%)	50 (42%)
CHA₂DS₂-VAsC score ≥2	-	62 (44%)	57 (31%)	86 (73%)
Oral anticoagulation therapy	-	63 (45%)	31 (17%)	70 (59%)
Acetylsalicylic acid	-	27 (19%)	28 (15%)	25 (21%)
Daily smoking ^b	45 (2%)	1 (1%)	0 (0%)	10 (9%)
Frequency of alcohol intake^b				
<once per month	282 (12%)	18 (13%)	26 (14%)	15 (13%)
>once per week	847 (38%)	50 (36%)	67 (36%)	63 (53%)
Leisure-time physical activity				
Sedate	222 (10%)	16 (11%)	20 (11%)	47 (40%)
Light	369 (16%)	26 (19%)	21 (11%)	48 (41%)
Moderate	1209 (53%)	75 (54%)	100 (54%)	22 (19%)
High	504 (22%)	23 (16%)	44 (24%)	1 (1%)
Engaged in regular exercise^c	1682 (73%)	90 (64%)	134 (72%)	26 (39%)
Still participating	776 (34%)	27 (19%)	52 (28%)	-

in the race^d

Reason for not

participating^d

Atrial fibrillation	-	50 (36%)	34 (18%)	-
Other disease	139 (6%)	8 (6%)	10 (5%)	-
Not motivated	657 (29%)	27 (19%)	42 (23%)	-
Reduced physical capacity	93 (4%)	11 (8%)	12 (6%)	-
Others	627 (27%)	17 (12%)	37 (20%)	-
Poor subjective health	128 (6%)	25 (18%)	24 (13%)	35 (31%)

AF = Atrial fibrillation.

^a Current. ^b During the previous 12 months. ^c Still engaged in regular endurance exercise (bouts of ≥ 30 minutes ≥ 3 times per week with the goal to improve or maintain endurance capacity).

^d Participating in the annually 54-kilometre Birkebeiner cross-country ski race.

Table 2: Physical activity, palpitations, functional capacity, use of rate-controlling drugs and subjective health according to atrial fibrillation subtype in veteran skiers and the general population aged 53-85 years,=253.

	Veteran skiers with AF (n=137)			General population with AF (n=116)		
	Non-permanent n=104 (%)	Permanent n=33 (%)	p-value	Non-permanent n=77 (%)	Permanent n=34 (%)	p-value
Physical activity ^a	78 (75%)	18 (55%)	<0.05	15 (19%)	7 (19%)	0.93
Palpitations ^b	65 (63%)	15 (46%)	0.09	57 (71%)	22 (61%)	0.28
Reduced capacity ^c	30 (29%)	14 (47%)	0.47	22 (28%)	16 (44%)	0.07
Rate-controlling drugs ^d	43 (43%)	15 (47%)	0.67	53 (70%)	28 (78%)	0.37
Poor subjective health	16 (16%)	8 (25%)	0.23	25 (33%)	9 (27%)	0.53

AF = Atrial fibrillation.

^a Moderate or high levels of leisure-time physical activity during the past year. ^b During the past year.

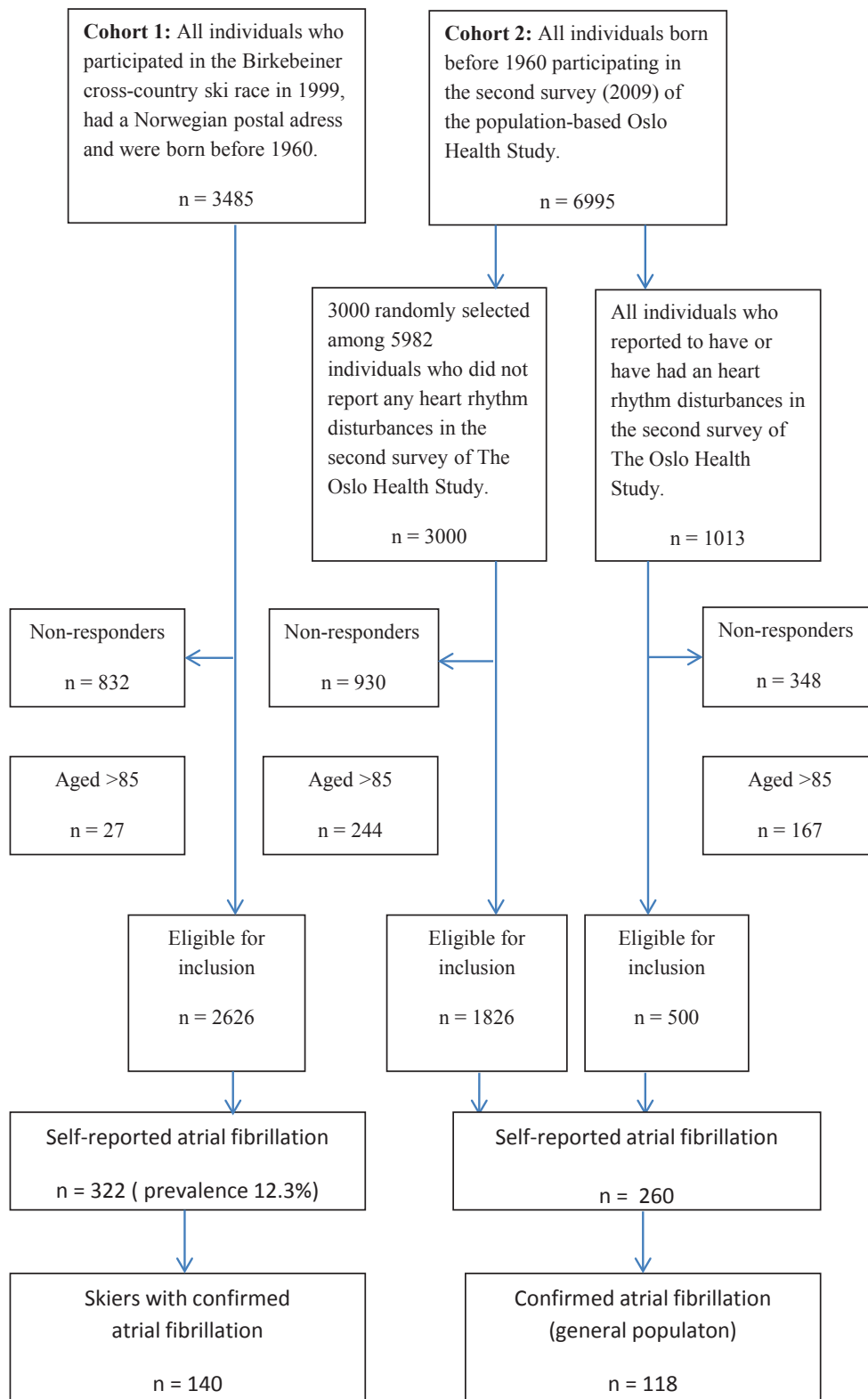
^c New York Heart Association class II-IV. ^d Drugs taken daily.

Table 3: Physical activity, palpitations, functional capacity, use of rate-controlling drugs and subjective health in individuals with atrial fibrillation according to co-morbid conditions. Men and women aged 53-85 years, n=258.

	Atrial fibrillation without co-morbid conditions	Atrial fibrillation with comorbid conditions ^e	p-value
	n=130	n= 128	
	(80 veteran skiers)	(60 veteran skiers)	
	(%)	(%)	
Physical activity ^a	69 (53%)	52 (41%)	<0.05
Palpitations ^b	85 (65%)	77 (60%)	0.39
Reduced capacity ^c	38 (29%)	46 (36%)	0.25
Rate-controlling drugs ^d	72 (58%)	69 (55%)	0.70
Poor subjective health	22 (18%)	38 (31%)	<0.05

Veteran skiers and individuals from the general population analyzed together. ^a Moderate or high levels of leisure-time physical activity during the past year. ^b During the past year. ^c New York Heart Association class II-IV. ^d Drugs taken daily. ^e Heart disease, diabetes, hyperthyroidism, acute infection or surgery during the past seven days (registered during the review of medical records). In individuals with hypertension the arrhythmia was classified as without co-morbidity if echocardiography findings were available and normal.

Supplementary figure 1: Inclusion process in the Birkebeiner Atrial Fibrillation Study



Appendices

ID number:

Date.....

The Birkebeiner Ageing Study (BiAS) - questionnaire

Part 1:

Age

Gender

☐ *Male*

☐ *Female*

Weight and height

Weight (kg).....

Height (cm).....

How many times have you completed the Birkebeiner cross country ski race?

How many times have you been awarded with the Birkebeiner Medal?

How old were you when you first attended?

Do you participate in other skiing events?

☐ *Yes*

☐ *No*

Do you participate in other bike competitions, cross country running race or street race?

☐ *Yes*

☐ *No*

At what age did you start with systematic training for the Birkebeiner cross country ski race (or other competitions)?

Have you had any interruption in training (more than 3 months) due to illness?

☐ *Yes*

☐ *No*

Have you ever been prevented from participating in the Birkebeiner cross country ski race due to illness?

☐ *Yes*

☐ *No*

What was the reason?

Do you have, or have you had atrial fibrillation (attack with rapid irregular heartbeat)?

☐ *Yes, once*

☐ *Yes, several times*

☐ *Yes, I have a chronic condition*

☐ *No*

Do you find that participation in Birkebeiner cross country ski race and the training it takes to affect your quality of life (well-being)?

- ☐ *For the better*
☐ *Has little impact*
☐ *For the worse*
☐ *Do not know*

Do you feel that participating in the Birkebeiner cross country ski race and the training it takes to affect the ageing process?

- ☐ *Makes me feel younger than my peers*
☐ *Makes no difference*
☐ *Makes me feel older than my peers*
☐ *Do not know*

If you look back at your life, what sport and what exercises did you start with?

.....

How old were you when you started with endurance training?

.....year

Part 2. CONOR- Health questionners YOUR OWN HEALTH

1. What is your current health status? Tick one only

- ☐ Poor
☐ Not so good
☐ Good
☐ Very good

2. Do you have, or have you had?

	Yes	No	Age first time
Heart attack			
Angina pectoris (heart cramp)			
Cerebral stroke/ Brain haemorrhage			
Asthma			
Diabetes			

3. Have you during the last year suffered from pain and/or stiffness in muscles and joints that have lasted for at least 3 months ?

- ☐ Yes ☐ No

4. Have you in the last two weeks felt :

	No	A little	A lot	Very much
Nervous or worried				
Anxious				
Confident and calm				
Irritable				
Happy/Optimistic				
Down/Depressed				
Lonely				

PHYSICAL ACTIVITY

5a. How has your physical activity during leisure time been over the last year ? *Think of your weekly average for the year. Time spent going to or from work counts as leisure time*

Hours per week	None	Less than 1	1-2	3 or more
Light activity (<i>not sweating or out of breath</i>)				
Hard physical activity (<i>sweating/out of breath</i>)				

5 b. Please note physical activity during the past year in your leisure time. If your activity level varies between summer and winter, note an average value.

(Tick one only)

- ☐ Reading, watching TV or any other sedentary activity?
- ☐ Walking, cycling, or other activity, other for at least 4 hours a week?
(Count also walking back and forth from work)
- ☐ Light sports, heavy gardening?
(At least 4 hours per week)
- ☐ Hard exercise, competitive sports? Regularly and several times a week

SMOKING

6 . How many hours a day do you normally spend in smoke-filled rooms? *Write 0 if you don't spend time in smoke-filled rooms*

Number of hours

7. Did any of the adults smoke at home when you grew up?

☐ Yes ☐ No

8. Do you now, or have you ever lived together with a daily smoker after the age of 20 years?

☐ Yes ☐ No

9. Do you smoke ?

	Yes	No
Cigarettes daily		
Cigars/cigarillos daily		
Pipe daily		

10. If you previously smoked daily, how long is it since you quit? number of years

11. If you smoke daily now or previously: How many cigarettes do you, or did you usually smoke per day? Number of cigarettes

12. How old were you when you began smoking? year

13. How many years in all have you smoked daily ? years

COFFEE, TEA AND ALCOHOL

14.a How many cups of coffee do you usually drink daily ?

Write 0 if you do not drink coffee daily

Boiled coffee (coarsely ground), number.....

Coffee other, number.....

14.b

What type of coffee do you usually drink? Please tick

- ☐ Filter/instant coffee
- ☐ Boiled coffee (coarsely ground)
- ☐ Other (espresso etc)
- ☐ Do not drink coffee

How many cups of coffee/tea do you usually drink daily? Write 0 if you do not drink coffee/tea daily

Number of cups with coffee.....

Number of cups with tea.....

15 a. How many times a month do you usually drink alcohol? Do not count low-alcohol beer. Put 0 if less than once a month.

Number of times.....

15 b. Approximately how often during the past 12 months have you consumed alcohol? (Do not count low-alcohol beer)

- ☐ 4-7 times a week ☐ 2-3 times a month ☐ Have not drunk alcohol the last year
- ☐ 2-3 times a week ☐ Appr. 1 time a month ☐ Have never drunk alcohol
- ☐ App. 1 time a week ☐ A few times last year

16 a. How many glasses of beer, wine or spirits do you usually drink during a two-weeks period? Do not count low-alcohol beer. Put 0 if you do not drink alcohol.

Beerglasses Wineglasses Spiritsglasses

For those who have consumed alcohol during the past year

16 b. When you drank alcohol, how many glasses did you usually drink ?

Number of glasses.....

16 c. Approximately how often during the past 12 months have you consumed alcohol corresponding to at least 5 glasses of spirits in 24 hours?

Number of times.....

16 d. When you drink alcohol, do you usually drink: (Tick one or more).

- ☐ Beer ☐ Wine ☐ Spirits (hard liquor)

16. Are you a total abstainer from alcohol?

- ☐ Yes ☐ No

EDUCATION

17 a. What is the highest level of education you have completed?

- ☐ Less than 7 year of primary school
- ☐ 7-10 years primary/secondary school
- ☐ Technical school, middle school, vocational school, 1-2 years senior high school

- ☐ High school diploma (3-4 years)
- ☐ College/university, less than 4 years
- ☐ College/university, 4 or more years

17 b. How many years education have you completed all together?

(Count every year you went to school) Number of years.....

ILLNESS IN THE FAMILY

18. Have one or more of your parents or siblings had a heart attack or angina pectoris?

- ☐ Yes ☐ No ☐ Don't know

19. Tick for those relatives who have or have had:

	Myself	Mot her	Fat her	Brot her	Sister	Chil d
Cerebral stroke or brain haemorrhage						
Myocardial infarction before age 60						
Asthma						
Cancer						
Diabetes						
Age when diabetes was first diagnosed						

RESIDENLY

20. In which municipality did you live at the age of 1 year? If you did not live in Norway, give country of residence instead of municipality.

21. What type of dwelling do you live in?

- ☐ Villa/detached house
- ☐ Farm
- ☐ Flat/apartment
- ☐ Terraced/semi-detached house
- ☐ Other/institution/care home

22. How large is your home?m²

FAMILY AND FRIENDS

25. With whom do you live? Tick one for each question and write the number

	Yes	No	Number
Spouse/Partner			
Other persons older than 18 years			
Persons younger than 18 years			

27. How many good friends do you have with whom you can talk confidentially and who can provide help if you need it?

(Do not count people you live with, but do include other relatives)

.....

28. Do you feel that you have enough good friends?

- ☐ Yes ☐ No

29. How often do you usually take part in organised activities, e.g. sewing circles, sports clubs, political meetings, religious or other organizations?

- ☐ Never, or just a few times a year
☐ 1-3 times a month
☐ Approximately once a week
☐ More than once a week

WORK

30. What is your current work situation?

- ☐ Paid work
☐ Full-time housework
☐ Under education, military service
☐ Unemployed, on leave without payment
☐ Pensioner

31 a. How many hours of paid work do you have per week?number of hours

31 b. What is your current work situation – paid work?

- ☐ Yes, full-time
☐ Yes, part time
☐ No

32. Do you receive any of the following?

- ☐ Sickness benefit?
☐ Old-age pension?
☐ Rehabilitation benefit?
☐ Disability pension?
☐ Unemployment benefits?
☐ Social welfare benefits?
☐ Social benefit-single parent?

33. Do you work shifts or nights?

- ☐ Yes ☐ No

34. If you have paid or unpaid work, which statement describes your work best?

- ☐ Mostly sedentary work? (*e.g. office work, mounting*)

☐ Work that requires a lot of walking? (*e.g. shop assistant, light industrial work, teaching*)

☐ Work that requires a lot of walking and lifting? (*e.g. postman, nursing, construction*)

☐ Heavy manual labour? (*e.g. forestry, heavy farmwork, heavy construction*)

35. Do you decide yourself how your work will be done? (Tick one only)

- ☐ Not at all
☐ Very little
☐ Yes, sometimes
☐ Yes, my own decision

36 a. Do you have any of the following occupations ? (full time or part time) Tick one for each question

	Yes	No
Driver		
Farmer		
Fisherman		

36 b. What occupation/title did you have at this work? Ex secretary, teacher, industrial worker, nursing, carpenter, leader, salesman, driver etc)

Occupation:.....

YOUR OWN ILLNESS and INJURIES

37. Have you ever had:

Tick one for each question. State age at event. If it has happened several times, write age at the last event.

	Yes	No	Age at last time
Hip fracture			
Wrist/forearm fracture			
Whiplash			
Injury requiring hospital admission			

38. Do you have or have you ever had?

Tick yes or no for each question

	Yes	No
Hay fever		
Chronic bronchitis/emphysema		
Osteoporosis		
Fibromyalgia/fibrositis/chronic pain syndrome		
Psychological problems for which you have sought help		

39. Do you cough almost daily for some periods of the year?

- ☐ Yes ☐ No

**40. If yes,
do you bring up phlegm?**

- ☐ Yes ☐ No

41. If you cough almost daily for some periods of the year, have you had this kind of cough for as long as 3 months in each of the last two years?

- ☐ Yes ☐ No

42. How often do you suffer from sleeplessness?

- ☐ Never, or just a few times a year
☐ 1-3 times a month
☐ Approximately once a week
☐ More than once a week

43. Have you in the last twelve months suffered from sleeplessness to the extent that it has affected your ability to work ?

- ☐ Yes ☐ No

USE OF MEDICATION

44 . Do you take?

	Currently	Previously	Never
Lipid lowering drugs			
Medications for high blood pressure			

45 a. Have you for any length of time in the past year used any of the following medications every day or almost daily? Indicate how many months you have used the medication. Write 0 if you did not take the medication.

Medications:

Painkillers months.
 Sleeping pills months.
 Tranquilizers months.
 Antidepressants months.
 Allergy pills months.
 Asthma medication months.

Only medication bought at pharmacy. Do not include dietary supplements.

45 b. How often during the last 4 weeks have you taken any of the following medication?

Tick one per line

	Daily	Weekly but not daily	Less than weekly	Not taken last 4 weeks
Painkillers without prescription				
Painkillers on prescription				
Sleeping pills				
Tranquilizers				
Antidepressants				
Other medication on prescription				

DIETARY SUPPLEMENTS

46 a. Have you for any length of time in the past year taken any of the following daily or almost daily? Indicate how many months you have used them. Write 0 if you did not take any.

Iron tablets months
 Vitamin D supplements months
 Other vitamin supplements months

Cod liver oil months

46 b. Do you take any of the following?

	Yes, daily	Sometimes	No
Cod liver oil, capsules, Fish oil capsules			
Vitamin and or mineral supplements			

THE REST OF THE FORM SHOULD ONLY BE FILLED IN BY WOMEN

47. How old were you when you started menstruating?

.....year

48. If you no longer menstruate, how old were you when you stopped menstruating?

.....year

50. How many children have you given birth to?

.....children

51. If you have given birth, what year was the child born and how many months did you breastfeed each child

Child	Year born	Number of months with breastfeeding
1.		
2.		
3.		
4.		
5.		
6.		

52. Do you use or have you ever used:

	Now	Previously	Never
Contraceptive pills (OC) (incl. minipill)			
Contraceptive injections			
Hormonal intrauterine device			
Estrogen (tablets or patches)			
Estrogen (cream or suppositories)			

International Physical Activity Questionnaire (IPAQ)

The questions will ask you about the time you spent being physically active in the **last 7 days**.

Activity Level		
Remember: Think only about those physical activities that you did for at least 10 minutes at a time.		
1a: During the last 7 days, on how many days did you do vigorous physical activities like heavy lifting, digging, aerobics, or fast bicycling,? Think about <i>only</i> those physical activities that you did for at least 10 minutes at a time.days per week	None (Skip to question 2a)
1b: How much time in total did you usually spend on one of those days doing vigorous physical activities?hoursminutes	
2a: Again, think <i>only</i> about those physical activities that you did for at least 10 minutes at a time. During the last 7 days, on how many days did you do moderate physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.days per week	None (Skip to question 3a)
2b: How much time in total did you usually spend on one of those days doing moderate physical activities?hoursminutes	
3a: During the last 7 days, on how many days did you walk for at least 10 minutes at a time? This includes walking at work and at home, walking to travel from place to place, and any other walking that you did solely for recreation, sport, exercise or leisure.days per week	None (Skip to question 4)
3b: How much time in total did you usually spend walking on one of those days?hoursminutes	
4: The last question is about the time you spent sitting on weekdays while at work, at home, while doing course work and during leisure time. This includes time spent sitting at a desk, visiting friends, reading traveling on a bus or sitting or lying down to watch television. During the last 7 days, how much time in total did you usually spend <i>sitting</i> on a week day ?		
hoursminutes	

SF-12

This survey asks for your views about your health. This information will help you keep track of how you feel and how well you are able to do your usual activities.

Answer every question by selecting the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

- ☐ *Excellent*
- ☐ *Very good*
- ☐ *Good*
- ☐ *Fair*
- ☐ *Poor*

2-3. The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much?

Activity	Yes, limited a lot	Yes, limited a little	No, not limited at all
2. <u>Moderate activities</u> , such as moving a table, pushing a vacuum cleaner, bowling, or playing golf			
3. Climbing <u>several</u> flights of stairs			

4- 5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

4. Accomplished less than you would like ☐ *Yes* ☐ *No*

5. Were limited in the kind of work or other activities ☐ *Yes* ☐ *No*

6-7. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

6. Accomplished less than you would like? ☐ *Yes* ☐ *No*

7. Did work or other activities less carefully than usual? ☐ *Yes* ☐ *No*

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

- ☐ *Not at all*
- ☐ *A little bit*
- ☐ *Moderately*
- ☐ *Quite a bit*
- ☐ *Extremely*

9-11. These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes close to the way you have been feeling. How much of the time during the past 4 weeks.

	All of the time	Most of the time	A good bit of the time	Some of the time	A little of the time	None of the time
9. Have you felt calm and peaceful?						
10. Did you have a lot of energy?						
11. Have you felt downhearted and blue?						

12. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

- ☐ All of the time
- ☐ Most of the time
- ☐ Some of the time
- ☐ A little of the time
- ☐ None of the time

Modified Health Assessment Questionnaire – MHAQ.

Please check the response that best describes your usual abilities OVER THE COURSE OF THE LAST WEEK.

Are you able to:	Without any difficulty	With some difficulty	With much difficulty	Unable to do
Dress yourself, including tying shoelaces and doing buttons?				
Get in and out of bed?				
Lift a full cup or glass to your mouth?				
Walk outdoors on flat ground?				
Wash and dry your entire body?				
Bend down to pick up clothing from the floor?				
Turn regular faucets on and off?				
Get in and out of a bus, car, train, or airplane?				

The self- esteem scale.

	Strongly agree	Agree	No disagreement/ agreement	Disagree	Strongly disagree
I feel that I have a number of good qualities					
All in all, I am inclined to feel that I am a failure					
I am able to do things as well as most other people					
I take a positive attitude toward myself					
I certainly feel useless at times					
I wish I could have more respect for myself					
I feel that I am a person of worth, at least on an equal plane with others					
I feel I do not have much to be proud of					
On the whole, I am satisfied with myself					
At times I think I am no good at all					

Mastery Scale

	Strongly agree	Agree	No disagreement/ agreement	Disagree	Strongly disagree
I have little control about things that happen to me					
What will happen in the future considerably depends on myself					
Some of my problems I can't seem to solve at all					
There is not much that I can do to change important things in my life					
I often feel helpless dealing with the problems of life					
Sometimes I feel like a play ball of life					
I can do almost everything, if I want to					

To what extent do you agree with the following statements about your relationship with your training and your relationship to activities like the Birkebeiner cross country ski race?

	Strongly disagree			Strongly agree
The sport means a lot to my quality of life				
Good sports performance means a lot to me				
Participation in the Birkebeiner cross country ski race is a motivation for practicing systematic				



Tromsø-undersøkelsen

The form will be read electronically. Please use a blue or black pen
You can not use comas, use upper-case letters.

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HEALTH AND DISEASES

1 How do you in general consider your own health to be?

- ☐ Very good
☐ Good
☐ Neither good nor bad
☐ Bad
☐ Very bad



2 How is your health compared to others in your age?

- ☐ Much better
☐ A little better
☐ About the same
☐ A little worse
☐ Much worse

3 Do you have, or have you had?

Yes No Age first time

- | | | | |
|---|--------------------------|--------------------------|----------------------|
| Heart attack | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Angina pectoris | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Stroke/brain hemorrhage | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Atrial fibrillation | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| High blood pressure | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Osteoporosis | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Asthma | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Chronic bronchitis/Emphysema/COPD | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Diabetes mellitus | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Psychological problems (for which you have sought help) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Low metabolism | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Kidney disease, not including urinary tract infection (UTI) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Migraine | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

4 Do you have persistent or constantly recurring pain that has lasted for 3 months or more?

- ☐ Yes ☐ No

5 How often have you suffered from sleeplessness during the last 12 months?

- ☐ Never, or just a few times
☐ 1-3 times a month
☐ Approximately once a week
☐ More than once a week



6 Below you find a list of different situations.

Have you experienced some of them in the last week (including today)? (Tick once for each complaint)

No Little Pretty Very
complaint complaint much much

- | | | | | |
|---|--------------------------|--------------------------|--------------------------|--------------------------|
| Sudden fear without reason | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| You felt afraid or worried | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Faintness or dizziness | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| You felt tense or upset | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Easily blamed yourself | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Sleeping problems | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Depressed, sad | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| You felt useless, worthless | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Feeling that life is a struggle | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Feeling of hopelessness with regard to the future | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

USE OF HEALTH SERVICES

7 Have you during the past year visited:

If YES; how many times?

Yes No No. of times

- | | | | |
|--|--------------------------|--------------------------|----------------------|
| General practitioner (GP) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Psychiatrist/psychologist | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Medical specialist outside hospital (other than general practitioner/psychiatrist) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Physiotherapist | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Chiropractor | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Alternative medical practitioner (homeopath, acupuncturist, foot zone therapist, herbal medical practitioner, laying on hands practitioner, healer, clairvoyant, etc.) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Dentist/dental service | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

8 Have you during the last 12 months been to a hospital?

Yes No No. of times

- | | | | |
|---|--------------------------|--------------------------|----------------------|
| Admitted to a hospital | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Had consultation in a hospital without admission; | | | |
| At psychiatric out-patient clinic | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| At another out-patient clinic | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

9 Have you undergone any surgery during the last 3 years?

- ☐ Yes ☐ No



USE OF MEDICINE

- 10 Do you take, or have you taken some of the following medications? (Tick once for each line)

	Never used	Now	Earlier	Age first time
Drugs for high blood pressure	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Lipid lowering drugs	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Drugs for heart disease	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Diuretics	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Medications for osteoporosis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Insulin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Tablets for diabetes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Drugs for metabolism	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Thyroxine/levaxin	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>

- 11 How often have you during the last 4 weeks used the following medications? (Tick once for each line)

	Not used the last 4 weeks	Less than every week	Every week, but not daily	Daily
Painkillers on prescription	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Painkillers non-prescription	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Sleeping pills	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tranquillizers	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Antidepressants	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- 12 State the names of all medications -both those on prescription and non-prescription drugs- you have used regularly during the last 4 weeks. Do not include vitamins, minerals, herbs, natural remedies, other nutritional supplements, etc.

If the space is not enough for all medications, use an additional paper of your own.

When attending the survey centre you will be asked whether you have used antibiotics or painkillers the last 24 hours. If you have, you will be asked to provide the name of the drug, strength, dose and time of use.

FAMILY AND FRIENDS

- 13 Who do you live with? (Tick for each question and give the number)

	Yes	No	Number
Spouse/cohabitant	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Other persons older than 18 years	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Persons younger than 18 years	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>

- 14 Tick for relatives who have or have had

	Parents	Children	Siblings
Myocardial infarction	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Myocardial infarction before 60 years	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Angina pectoris	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Stroke/brain haemorrhage	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Osteoporosis	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Stomach/duodenal ulcer	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Asthma	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Diabetes mellitus	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Dementia	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Psychological problems	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Drugs/substance abuse	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

- 15 Do you have enough friends who can give you help when you need it?

☐ Yes ☐ No

- 16 Do you have enough friends whom you can talk confidentially with?

☐ Yes ☐ No

- 17 How often do you normally take part in organised gatherings, e.g. sports clubs, political meetings, religious or other associations?

☐ Never, or just a few times a year

☐ 1-2 times a month

☐ Approximately once a week

☐ More than once a week

WORK, SOCIAL SECURITY AND INCOME

- 18 What is the highest level of education you have completed? (Tick one)

☐ Primary, 1-2 years secondary school

☐ Vocational school

☐ High secondary school (A-level)

☐ College/university less than 4 years

☐ College/university 4 years or more

- 19 What is your main occupation/activity? (Tick one)

☐ Full time work ☐ Housekeeping

☐ Part time work ☐ Retired/benefit recipient

☐ Unemployed ☐ Student/military service

20 Do you receive any of the following benefits?

- ☐ Old-age, early retirement or survivor pension
☐ Sickness benefit (are in a sick leave)
☐ Rehabilitation benefit
☐ Full disability pension
☐ Partial disability pension
☐ Unemployment benefits
☐ Transition benefit for single parents
☐ Social welfare benefits

21 What was the households total taxable income last year? Include income from work, social benefits and similar

- ☐ Less than 125 000 NOK ☐ 401 000-550 000 NOK
☐ 125 000-200 000 NOK ☐ 551 000-700 000 NOK
☐ 201 000-300 000 NOK ☐ 701 000 -850 000 NOK
☐ 301 000-400 000 NOK ☐ More than 850 000 NOK

22 Do you work outdoors at least 25% of the time, or in cold buildings (e.g. storehouse/industry buildings)?

- ☐ Yes ☐ No

PHYSICAL ACTIVITY

23 If you have paid or unpaid work, which statement describes your work best?

- ☐ Mostly sedentary work
(e.g. office work, mounting)
☐ Work that requires a lot of walking
(e.g. shop assistant, light industrial work, teaching)
☐ Work that requires a lot of walking and lifting
(e.g. postman, nursing, construction)
☐ Heavy manual labour

24 Describe your exercise and physical exertion in leisure time. If you activity varies much, for example between summer and winter, then give an average. The question refers only to the last year. (Tick the one that fits best)

- ☐ Reading, watching TV, or other sedentary activity.
☐ Walking, cycling, or other forms of exercise at least 4 hours a week *(here including walking or cycling to place of work, Sunday-walking, etc.)*
☐ Participation in recreational sports, heavy gardening, etc. *(note: duration of activity at least 4 hours a week)*
☐ Participation in hard training or sports competitions, regularly several times a week.

25 How often do you exercise? (With exercise we mean for example walking, skiing, swimming or training/sports)

- ☐ Never
☐ Less than once a week
☐ Once a week
☐ 2-3 times a week
☐ Approximately every day

26 How hard do you exercise on average?

- ☐ Easy- do not become short-winded or sweaty
☐ You become short-winded and sweaty
☐ Hard- you become exhausted

27 For how long time do you exercise every time on average?

- ☐ Less than 15 minutes ☐ 30-60 minutes
☐ 15-29 minutes ☐ More than 1 hour

ALCOHOL AND TOBACCO

28 How often do you drink alcohol?

- ☐ Never
☐ Monthly or more infrequently
☐ 2-4 times a month
☐ 2-3 times a week
☐ 4 or more times a week

29 How many units of alcohol (a beer, a glass of wine or a drink) do you usually drink when you drink alcohol?

- ☐ 1-2 ☐ 5-6 ☐ 10 or more
☐ 3-4 ☐ 7-9

30 How often do you drink 6 units of alcohol or more in one occasion?

- ☐ Never
☐ Less frequently than monthly
☐ Monthly
☐ Weekly
☐ Daily or almost daily

31 Do you smoke sometimes, but not daily?

- ☐ Yes ☐ No

32 Do you/did you smoke daily?

- ☐ Yes, now ☐ Yes, previously ☐ Never

33 If you previously smoked daily, how long is it since you stopped?

Number of years

34 If you currently smoke, or have smoked before: How many cigarettes do you or did you usually smoke per day?

Number of cigarettes

35 How old were you when you began smoking daily?

Number of years

36 How many years in all have you smoked daily?

Number of years

37 Do you use or have you used snuff or chewing tobacco?

- ☐ No, never ☐ Yes, sometimes
☐ Yes, previously ☐ Yes, daily

DIET

38 Do you usually eat breakfast every day?

☐ Yes ☐ No

39 How many units of fruits or vegetables do you eat on average per day? (units means for example a fruit, a cup of juice, potatoes, vegetables)

Number of units +

40 How many times per week do you eat hot dinner?

Number

41 How often do you usually eat these products? (Tick once for each line)

	0-1 times/ mth	2-3 times/ mth	1-3 times/ week	4-6 times/ week	1-2 times/ day
Potatoes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pasta/rice	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Meat (not processed)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Processed meat (sausages/meatloaf/meatballs)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fruits, vegetables, berries	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lean fish	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fat fish (e.g. salmon, trout, mackerel, herring, halibut, redfish)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

42 How much do you normally drink the following? (Tick once for each line)

	Rarely/ never	1-6 glasses /week	1 glass /day	2-3 glasses /day	4 or more glasses /day
Milk, curdled milk, yoghurt	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Juice	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Soft drinks with sugar	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

43 How many cups of coffee and tea do you drink daily? (Put 0 for the types you do not drink daily)

	Number of cups
Filtered coffee	<input type="text"/> <input type="text"/>
Boiled coffee (coarsely ground coffee for brewing)	<input type="text"/> <input type="text"/>
Other types of coffee	<input type="text"/> <input type="text"/>
Tea	<input type="text"/> <input type="text"/>

44 How often do you usually eat cod liver and roe? (i.e. "mølje")

☐ Rarely/never ☐ 1-3 times/year ☐ 4-6 times/year
☐ 7-12 times/year ☐ More than 12 times/year

45 Do you use the following supplements?

	Daily	Sometimes	No
+ Cod liver oil or fish oil capsules	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Omega 3 capsules (fish oil, seal oil)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vitamins and/or mineral supplements	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

QUESTIONS FOR WOMEN

46 Are you currently pregnant?

☐ Yes ☐ No ☐ Uncertain

47 How many children have you given birth to?

Number +

48 If you have given birth, fill in for each child: birth year, birth weight and months of breastfeeding (Fill in the best you can)

Child	Birth year	Birth weight in grams	Months of breastfeeding
1	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
2	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
3	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
4	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
5	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>
6	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	<input type="text"/> <input type="text"/>

49 During pregnancy, have you had high blood pressure?

☐ Yes ☐ No

50 If yes, which pregnancy?

☐ The first ☐ Second or later

51 During pregnancy, have you had proteinuria?

☐ Yes ☐ No

52 If yes, which pregnancy?

☐ The first ☐ Second or later

53 Were any of your children delivered prematurely (a month or more before the due date) because of preeclampsia?

☐ Yes ☐ No

54 If yes, which child?

1st child 2nd child 3rd child 4th child 5th child 6th child
☐ ☐ ☐ ☐ ☐ ☐

55 How old were you when you started menstruating?

Age +

56 Do you currently use any prescribed drug influencing the menstruation?

Oral contraceptives, hormonal IUD or similar

☐ Yes ☐ No

Hormone treatment for menopausal problems



☐ Yes ☐ No

When attending the survey centre you will get a questionnaire about menstruation and possible use of hormones. Write down on a paper the names of all the hormones you have used and bring the paper with you. You will also be asked whether your menstruation have ceased and possibly when and why.

Birkebeiner Atrial Fibrillation Study

This form shall be read by a machine.

It is therefore important that you:

- Use a blue or black pen
- Make a cross like this , and not like this 
- Write numbers in the following manner:

0	1	2	3	4	5	6	7	8	9
---	---	---	---	---	---	---	---	---	---

ABOUT YOU

1. Gender Female Male
2. Age years
3. Height cm
4. Weight kg
5. Who do you live together with?

Live alone Spouse/partner Other people 18 years of age and older People under 18 years of age

HEALTH

6. How is your health currently?

Poor Fair Good Excellent

7. Do you suffer from or have you ever suffered from the following illnesses?
(Insert a cross and age when first occurred)

	Yes	No	Age when first occurred	Confirmed by doctor	
				Yes	No
Myocardial infarct					
Angina pectoris					
Hyperthyroidism					
Diabetes					
Operated heart valve					
Heart bypass operation					
High blood pressure					
High cholesterol					
Stroke					
Asthma					

8. If you have a heart disease, how does it impact on your ability to function?
No restrictions. Normal physical activity causes no unusual fatigue, shortness of breath or chest pains.

Slight restriction on physical activity, however unaffected when resting. Normal physical activity causes fatigue, shortness of breath or chest pains.

Significant restrictions on physical activity. Even minor physical exertion causes fatigue, shortness of breath or chest pains.

Impossible to perform any type of physical activity. In periods, also shortness of breath or chest pains when resting.

9. Do you use or have you used (insert cross)

	Yes, now	Previously, but no longer	Never
Blood pressure-lowering medicines			
Cholesterol-reducing medicines			
Inhalation medication against asthma or chronic obstructive pulmonary disease (COPD)			

10. Have you had continual muscle or skeletal pains for at least 3 months? Yes No

11. Have you used anti-inflammatory medicines over an extended period at least once in your life (Voltaren, Diclofenac, Brexidol, Naproxen, Naprosyn, Vioxx, Celebra, Ibux, Ibuprofen or similar)? Yes No

At least 2 consecutive weeks

At least 4 consecutive weeks

At least 8 consecutive weeks

At least 3 consecutive months

At least 6 consecutive months

TOBACCO

12. Do you smoke daily or have you previously smoked daily (cigarettes)?

Yes, now Yes, previously Never

13. If yes, how many cigarettes do/did you normally smoke per day? Number:

14. For how many years in total have you smoked/did you smoke daily? Number:

15. Do you use or have you used snus?

Yes, now Yes, previously Never

16. For how many years in total have you used/did you use snuff? Number:

ALCOHOL

17. Are you a complete teetotaler?

Yes, now Yes, have always been teetotal No

If you have always been teetotal, go directly to question 22.

18. Approximately how often have you consumed alcohol in the past year?

(Light beer and alcohol-free beer are not included)
Insert a cross in the appropriate box.

4-7 times per week	2-3 times per week	Approx. once per week	2-3 times per month	About once per month	A few times in the past year	Not in the past year	Never
-----------------------	-----------------------	-----------------------------	---------------------------	----------------------------	---------------------------------------	----------------------------	-------

19. How many glasses of the following drinks do you normally consume in a 2 week period?
 Beer Number
 Wine Number
 Spirits Number
20. When you have consumed alcohol, how many glasses and/or drinks have you normally had?
 Number
21. Approximately how many times during the past year have you drunk as much as at least 5 glasses/drinks during a 24 hour period? Number

STRESS

22. Insert a cross for the alternative that best describes your situation (only one cross for the **“At home”** and one cross for the **“At work”** column). By stress we mean that one feels tense, nervous, anxious or has problems with sleeping due to circumstances at home or at work.

	At home	At work
Have never experienced stress		
Have sometimes experienced stress		
Have experienced stress during the past 5 years		
Have experienced several periods of stress during the past 5 years		
Have experienced persistent stress in the past year		
Have experienced persistent stress in the past 5 years		

PHYSICAL ACTIVITY AND EXERCISE

23. State the movement and physical activity you engage in during your leisure time. If the level of activity varies significantly, e.g. between summer and winter, use an average. The question applies to the past 12 months.

(Insert a cross in the most appropriate box)

Reading, sitting still or other sedentary activities

Walking, cycling or other manner of movement 2-4 hours per week

Walking, cycling or other manner of movement at least 4 hours per week

Recreational exercise, heavier garden work or the like. (Note that the activity must be for at least 4 hours per week).

Hard exercise or competitive sport on a regular basis and several times per week.

24. Have you at any time in your life engaged in regular endurance exercise (exercise sessions for a minimum of 30 minutes at least 3 times per week with the goal of better endurance)?

Yes No

If yes, proceed to question 25

If no, go directly to question 34

25. How old were you when you started regular endurance exercise? Age:

26. How many years in total have you engaged in regular endurance exercise with the goal of better endurance?

Less than 5 years	5-9 years	10-19 years	20-29 years	30-39 years	40-49 years	50-59 years	More than 60 years

27. Approximately how many times per week on average have you engaged in endurance exercise during these years?

(Insert only one cross per row) Hours per week

Age period	< 2 hours	2-3 hours	4-5 hours	6-7 hours	More than 7 hours
11-15					
16-20					
21-30					
31-40					
41-50					
51-60					
Over 60					

28. What type of endurance exercise have you mostly been engaged in?

Mostly sessions with low intensity (heart rate <75% of max heart rate or able to conduct a conversation)

Mostly sessions with high intensity (heart rate >75% of max heart rate, e.g. interval training)

About half of the sessions at low intensity and half at high intensity

29. On average, how many times per week have you exercised at high intensity in the past year?

30. On average, how many times per week have you exercised at low intensity in the past year?

31. Do you still engage in regular endurance exercise?

Yes No

32. How many times in the course of your life have you engaged in endurance exercise even though you had a noticeable cold, an infection or fever?

Never Less than 5 times 5-15 times More than 15 times

33. How many times in the course of your life have you competed in endurance sport even though you had a noticeable cold, an infection or fever?

Never Once 2-3 times 4-5 times More than 5 times

PARTICIPATION IN THE BIRKEBEINER RACE

34. Have you competed in the Birkebeiner ski race?

Yes No

If yes, proceed to question 35

If no, go directly to question 41

35. How many times have you competed in the Birkebeiner race? Number:

36. How many times have you achieved the Birkebeiner Medal (Merket)? Number:

37. How old were you the first time you competed?

IF YOU HAVE STOPPED COMPETING IN THE BIRKEBEINER RACE:

38. How old were you when you competed for the last time? Age:

39. What was the most important reason for you no longer competing?

Atrial fibrillation

Heart attack

Other illness

No longer motivated

Had no desire due to being in poorer physical condition than previously

Other

40. Do you still compete in sporting competitions other than the Birkebeiner race? Yes No

ATRIAL FIBRILLATION

41. Have you noticed instances of sudden changes in pulse or heart rhythm in the past year?

Yes No

42. Do you believe yourself that you have or have had atrial fibrillation (heart fibrillation)?

Yes No Don't know

43. If yes, have you been diagnosed as suffering from atrial fibrillation by a doctor?

Yes No Don't know

44. If yes, where?

Regular doctor Hospital doctor

Name of the hospital.....

45. Do you suffer from persistent or paroxysmal atrial fibrillation?

(a) Have atrial fibrillations the entire time (b) Have/have had incidences that end by themselves or with tablet treatment.

(c) Have/have had incidences that are only alleviated by intravenous treatment or electric shock.

46. How often on average do you experience such incidences?

2 or more times per week About once per week 1-3 times per month Less than once per month

47. The incidences occur most often:

During exercise/physical exertion

After exercise/physical exertion

At night

In connection with stress

During or after consuming alcohol

After large meals

In connection with infections/fever

Without any clear connection with any of the above alternatives

48. When did you experience your first incidence of atrial fibrillations?

Month and year (e.g. 03.76)

49. When were you diagnosed as suffering from atrial fibrillations?

Month and year (e.g. 03.76)

50. Do you use the following medicines as a result of atrial fibrillations?

	Use	Have used
Beta blockers daily (e.g. Zelo-Zok, Metoprolol, Sotalol, Sotacor, Emconcor)		
Beta blockers in the event of an attack		
Calcium blocks daily (e.g. Isoptin, Verapamil, Veracard)		
Calcium blockers in the event of an attack		
Cordarone daily		
Cordarone in the event of an attack		
Tambocor/Flecainide daily		
Tambocor/Flecainide in the event of an attack		
Digitoxin/Digoxin/Lanoxin		
Albaryl-E/Magnyl-E/Acetylsalicylic acid		
Multaq/Dronedaron		
Marevan		
Dabigatran/Pradaxa		

51. Does anyone in your immediate family suffer from atrial fibrillation? (Insert cross)

Mother Father Sibling Child

52. How many times during your life (until you began to suffer from atrial fibrillation) have you used anti-inflammatory medicines more than once per day for at least a week at a time (Voltaren, Diclofenac, Brexidol, Naproxen, Naprosyn, Vioxx, Celebra, Ibux, Ibuprofen or similar)?

Never Less than 5 times 5-15 times More than 15 times Don't know

EDUCATION AND INCOME

53. What is the highest level of education you completed?

9 years or less of elementary school
High school graduate/upper secondary school
Less than 4 years' college/university education
4 Years or more of college/university education

54. How many years of education have you completed?
Include all the years you went to school or studied. Number:

54. What was your total gross income in the past year?
(Pensioners: What was your combined gross income BEFORE YOU RETIRED)?

NOK

Birkebeiner Aldringsstudien

Skjemaet skal leses av en maskin.

Det er derfor viktig at du:

- Bruker blå eller sort kulepenn
- Setter kryss ☒, ikke slik ☒
- Skriver tallene slik

0	1	2	3	4	5	6	7	8	9
---	---	---	---	---	---	---	---	---	---

OM DEG

1. Kjønn Kvinne ☐ Mann ☐

2. Alder år

3. Høyde cm

4. Vekt kg

5. Hvem bor du sammen med?

Ingen	Ektefelle/ Samboer	Andre personer 18 år og eldre	Personer under 18 år
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

HELSE

6. Hvordan er helsen din nå?

Dårlig	Ikke helt god	God	Svært god
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

7. Har du eller har du hatt følgende sykdommer:
(sett kryss og alder første gang.)

	Ja	Nei	Alder første gang	Bekreftet av lege Ja Nei
Hjerteinfarkt	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>
Angina pectoris	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>
Høyt stoffskifte/hypertyreose	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>
Sukkersyke/diabetes	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>
Operasjon av hjerteklaff	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>
Bypass-operasjon i hjertet	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>
Høyt blodtrykk	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>
Høyt kolesterol	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>
Hjerneslag	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>
Astma	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>	<input type="checkbox"/> <input type="checkbox"/>

8. Hvis du har hjertesykdom, hvordan virker dette på ditt funksjonsnivå?

Ingen begrensninger. Vanlig fysisk aktivitet gir ingen uvanlig tretthet, tungpust eller brystmerter.	<input type="checkbox"/>
Lett begrensning av fysisk aktivitet, men ubesværet i hvile. Vanlig fysisk aktivitet gir tretthet, tungpust eller brystmerter.	<input type="checkbox"/>
Betydelige begrensninger i fysisk aktivitet. Selv små fysiske anstrengelser gir tretthet, tungpust eller brystmerter.	<input type="checkbox"/>
Umulig å utføre noen som helst fysisk anstrengelse. Periodevis også tungpust eller brystmerter i hvile.	<input type="checkbox"/>

9. Bruker du eller har du brukt: (sett kryss)

	Ja, nå	For, men ikke nå	Aldri
Blodtrykksenkende medisiner	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Kolesterolsenkende medisiner	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Inhalasjonsmedisin mot astma eller kols	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

10. Har du i minst 3 måneder sammenhengende hatt muskel- eller skjelettsmerter? Ja ☐ Nei ☐

11. Har du brukt betennelsesdempende medisiner over en lengre periode minst en gang i livet (Voltaren, Diclofenac, Brexidol, Naproxen, Naprosyn, Vioxx, Celebra, Ibux, Ibuprofen el. lignende)? Ja ☐ Nei ☐

Minst 2 uker sammenhengende	<input type="checkbox"/>
Minst 4 uker sammenhengende	<input type="checkbox"/>
Minst 8 uker sammenhengende	<input type="checkbox"/>
Minst 3 måneder sammenhengende	<input type="checkbox"/> T
Minst 6 måneder sammenhengende	<input type="checkbox"/>

TOBAKK

12. Røyker du daglig eller har du tidligere røyket daglig (sigaretter)?

Ja, nå	Ja, tidligere	Aldri
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

13. Hvis ja, hvor mange sigaretter røyker eller røykte du vanligvis daglig?

Antall:

14. Hvor mange år har du til sammen røyket daglig?

Antall:

15. Bruker du eller har du brukt snus?

Ja, nå	Ja, tidligere	Aldri
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

16. Hvor mange år har du til sammen brukt snus?

Antall:

ALKOHOL

17. Er du total avholdsmann/-kvinne?

Ja, nå ☐ Ja, har alltid vært avholds ☐ Nei ☐

Hvis du alltid har vært avholdsmann/-kvinne gå direkte til spørsmål 22.

18. Omtrent hvor ofte har du i løpet av det siste året drukket alkohol?

(Lettøl og alkoholfritt øl regnes ikke med). Sett kryss i passende rute.

4-7 ganger i uka ☐ 2-3 ganger i uka ☐ Ca. 1 gang i uka ☐ 2-3 ganger pr. mnd. ☐ Omtrent 1 gang pr. mnd. ☐ Noen få ganger siste år ☐ Ikke siste år ☐ Aldri ☐

19. Hvor mange glass drikker du vanligvis i løpet av 2 uker av:

Øl	Antall:	<input type="text"/>
Vin	Antall:	<input type="text"/>
Brennevin	Antall:	<input type="text"/>

20. Når du har drukket alkohol, hvor mange glass/og eller drinker har du vanligvis drukket?

Antall:

21. Omtrent hvor mange ganger i løpet av det siste året har du drukket så mye som minst 5 glass/drinker i løpet av ett døgn?

Antall:

STRESS

22. Sett kryss for det alternativet som passer best for din situasjon (kun ett kryss for kolonnen "Hjemme" og ett kryss for kolonnen "På jobb".) Med stress mener vi at man kjenner seg spent, nervøs, engstelig eller har problemer med søvnen på grunn av forhold hjemme eller på jobb.

	Hjemme	På jobb
Har aldri opplevd stress	<input type="checkbox"/>	<input type="checkbox"/>
Har opplevd stress noen ganger	<input type="checkbox"/>	<input type="checkbox"/>
Har opplevd stress i løpet av de 5 siste årene	<input type="checkbox"/>	<input type="checkbox"/>
Har opplevd flere stressperioder de 5 siste årene	<input type="checkbox"/>	<input type="checkbox"/>
Har opplevd vedvarende stress det siste året	<input type="checkbox"/>	<input type="checkbox"/>
Har opplevd vedvarende stress de siste 5 årene	<input type="checkbox"/>	<input type="checkbox"/>

FYSISK AKTIVITET OG TRENING

23. Angi bevegelse og kroppslig anstrengelse i din fritid. Hvis aktiviteten varierer mye, for eksempel mellom sommer/vinter, så ta et gjennomsnitt. Spørsmålet gjelder bare de 12 siste månedene.

(Sett kryss i den ruten som passer best)

Leser, sitter stille eller annen stillesittende beskjeftigelse	<input type="checkbox"/>
Spaserer, sykler eller beveger deg på annen måte 2-4 timer i uken	<input type="checkbox"/>
Spaserer, sykler eller beveger deg på annen måte minst 4 timer i uken	<input type="checkbox"/>
Driver mosjonsidrett, tyngre hagearbeid eller lignende (Merk at aktiviteten skal være minst 4 timer i uken)	<input type="checkbox"/>
Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uken	<input type="checkbox"/>

24. Har du noen gang i livet drevet regelmessig utholdenhetstrening (treningsokter med varighet på minst 30 minutter minst 3 ganger i uken med mål om å bedre utholdenhet)?

Ja ☐ Nei ☐

Hvis ja, fortsett med spørsmål 25

Hvis nei, gå direkte til spørsmål 34

25. Hvor gammel var du da du begynte med regelmessig utholdenhetstrening?

Alder:

26. Hvor mange år tilsammen har du drevet regelmessig utholdningstrening flere ganger i uken med mål om å bedre utholdenheten?

Under 5 år	5-9 år	10-19 år	20-29 år	30-39 år	40-49 år	50-59 år	Mer enn 60 år
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

27. Omtrent hvor mange timer i uka har du gjennomsnittlig drevet utholdenhetstrening i løpet av disse årene?

(Sett kun ett kryss i hver rad) Timer pr. uke

Aldersperiode	< 2t	2-3t	4-5t	6-7t	mer enn 7 timer
11-15 år	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
16-20 år	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
21-30 år	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
31-40 år	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
41-50 år	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
51-60 år	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Over 60 år	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

28. Hva slags type utholdenhetstrening har du drevet mest med?

Flest økter med lav intensitet (puls <75% av maks puls, eller i stand til å føre en samtale)

☐

Flest økter med høy intensitet (puls >75% av maks puls, for eksempel intervalltrening.)

☐

Omtrent halvparten av øktene med lav intensitet og halvparten med høy intensitet

☐

T

29. I snitt hvor mange ganger i uken har du trent med høy intensitet det siste året?

30. I snitt hvor mange ganger i uken har du trent med lav intensitet det siste året?

31. Driver du fortsatt med regelmessig utholdenhetstrening?

Ja

Nei

☐☐

32. Hvor mange ganger i løpet av livet har du trent utholdenhetstrening selv om du har vært merkbart forkjølet, hatt en infeksjon eller hatt feber?

Aldri

☐

Mindre enn 5 ganger

☐

5-15 ganger

☐

mer enn 15 ganger

☐

33. Hvor mange ganger i løpet av livet har du deltatt i konkurranse i utholdenhetssidrett selv om du har vært merkbart forkjølet, hatt en infeksjon eller feber?

Aldri

☐

En gang

☐

2-3 ganger

☐

4-5 ganger

☐

Mer enn 5 ganger

☐

DELTAKELSE I BIRKEBEINERENNET

34. Har du deltatt i Birkebeinerrennet på ski?

Ja

Nei

☐☐

Hvis ja, fortsett med spørsmål 35
Hvis nei, gå direkte til spørsmål 41

35. Hvor mange ganger har du gått Birkebeinerrennet?

Antall:

36. Hvor mange ganger har du gått til Merket?

Antall:

37. Hvor gammel var du første gang du deltok?

Alder:

HVIS DU HAR SLUTTET Å DELTA I BIRKEBEINERENNET:

38. Hvor gammel var du da du deltok siste gang?

Alder:

39. Hva var den viktigste årsaken til at du sluttet å delta?

Atrieflimmer

☐

Hjerteinfarkt

☐

Annen sykdom

☐

Ikke motivert lenger

☐

Orket ikke på grunn av dårligere fysisk form enn før

☐

Annet

☐

40. Deltar du fortsatt i andre mosjonskonkurranser enn Birkebeinerrennet?

Ja

Nei

☐☐

ATRIEFLIMMER

41. Har du merket anfall med plutselig endring i pulsen eller hjerterytmen siste året?

Ja

Nei

☐☐

42. Mener du selv at du har eller har hatt atrieflimmer (forkammerflimmer/hjerteflimmer)?

Ja

Nei

Vet ikke

☐☐☐

Hvis nei gå til spørsmål 53

43. Hvis ja, har du fått stilt diagnosen atrieflimmer hos lege?

Ja

Nei

Vet ikke

☐☐☐

44. Hvis ja, hvor?

fastlege

lege på sykehus,

☐☐

Navn på sykehus.....

45. Har du permanent eller anfallsvis atrieflimmer?

a) har atrieflimmer hele tiden (permanent)

☐

b) har/har hatt anfall som går over av seg selv eller med tablettbehandling

☐

c) har/har hatt anfall som kun går over med intravenøs behandling eller elektrosjokk

☐

46. Hvor ofte har du i snitt anfa

2 eller flere ganger pr. uke	omtrent 1 gang pr. uke	1-3 ganger pr. mnd.	Sjeldnere enn 1 gang pr. mnd
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
T			

47. Anfalletne op er oftest:

under trening/fysiske anstrengelser	<input type="checkbox"/>
etter trening/fysiske anstrengelser	<input type="checkbox"/>
om natten	<input type="checkbox"/>
i forbindelse med stress	<input type="checkbox"/>
under eller etter inntak av alkohol	<input type="checkbox"/>
etter større måltider	<input type="checkbox"/>
i forbindelse med infeksjoner/feber	<input type="checkbox"/>
uten tydelig sammenheng med noen av alternativene ovenfor	<input type="checkbox"/>

48. Når hadde du ditt første an med atrieflimmer?

Mnd. og år (f. eks. 03.76)

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49. Når ble diagno atrieflimmer stilt?

Mnd. og år (f. eks. 03.76)

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50. Bruker du følgende medikamenter på grunn atrieflimmer? (Sett kryss)

	Bruker	Har brukt
Betablokker daglig (F.eks Zelo-Zok, Metoprolol, Sotalol, Sotacor, Emconcor)	<input type="checkbox"/>	<input type="checkbox"/>
Betablokker ved anfall	<input type="checkbox"/>	<input type="checkbox"/>
Kalsiumblokker daglig (F.eks Isoptin, Verapamil, Veracard)	<input type="checkbox"/>	<input type="checkbox"/>
Kalsiumblokker ved anfall	<input type="checkbox"/>	<input type="checkbox"/>
Cordarone daglig	<input type="checkbox"/>	<input type="checkbox"/>
Cordarone ved anfall	<input type="checkbox"/>	<input type="checkbox"/>
Tambocor/Flecainid daglig	<input type="checkbox"/>	<input type="checkbox"/>
Tambocor/Flecainid ved anfall	<input type="checkbox"/>	<input type="checkbox"/>
Digitoxin/Digoxin/Lanoxin	<input type="checkbox"/>	<input type="checkbox"/>
Albyl-E/Magnyl-E/Acetylsalisylsyre	<input type="checkbox"/>	<input type="checkbox"/>
Multaq/Dronedarone	<input type="checkbox"/>	<input type="checkbox"/>
Marevan	<input type="checkbox"/>	<input type="checkbox"/>
Dabigatran/Pradaxa	<input type="checkbox"/>	<input type="checkbox"/>

51. Har noen av dine e familiemedlemmer atrieflimmer? (Sett kryss)

mor	far	søsken	barn
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

52. Hvor mange ganger i løpet av livet (fram til du atrieflimmer) har du brukt betennelsesdempende medisiner flere ganger daglig i minst en uke av gangen (Voltaren, Diclofenac, Brexidol, Naproxen, Naprosyn, Vioxx, Celebra, Ibux, Ibuprofen el. lignende)?

aldri	mindre enn 5 ganger	5-15 ganger	mer enn 15 ganger	Vet ikke
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

UTDANNING OG INNTEKT

53. Hvilken utdanning er den høyeste du har fullfø

9 år grunnskole eller mindre	<input type="checkbox"/>
artium/videregående skole	<input type="checkbox"/>
mindre enn 4 år høyskole/universitetsutdanning	<input type="checkbox"/>
4 år eller mer på høyskole/universitet	<input type="checkbox"/>

54. Hvor mange års skolegang har du gjennomfø

Ta med alle år du har gått på skole eller studert.

Antall:

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55. Hva var din samlede brutto inntekt siste (Pensjonister: Hva var din samlede brutto inntekt FØR DU BLE PENSJONIST)?

Kr.

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IKKE SETT KRYSS HER (fylles ut av mottaker.)

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